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## DERMATOLOGY IN THE ARMY

CHAIRMAN'S ADDRESS

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War calls for unselfish effort and sacrifice on the part of every one. This particular war will drain our resources of money, men and material and will tax the skill and brain power of the country immeasurably. American medicine has already contributed a good share in skill and talent to the military efforts and is now cooperating well on the realization of a program of distributing itself equably to care for military, civilian and industrial needs. The military needs naturally are to be satisfied first with those best qualified for such duty. This will throw added burdens and duties on those who are left to care for the civilians. The whole program will result in a readjustment of every one's manner of living or conduct of business, and there will be no easy berth for any one—not even the slacker. The effort has to be extreme, and the only ones immune from the pinching effects of it should be institutionalized psychopathic patients and babes in arms.

When called into service, the first lesson for a dermatologist to realize is that he is a doctor and will be used as such. He has defined himself as an "internist who knows the skin," and he will be challenged accordingly. This is not meant to indicate that specialists are not needed and will not be used as such in the armed forces, for every specialist will be of value. However, the plans of organization call for a distribution of medical officers according to where physicians are needed and what is most expedient. These requisites are to be satisfied first before a physician can be expected to be put into a limited field wherein he does nothing but the work that he did in civil life. This is no time for any of us to indulge in any misgivings, whether we are civilians or in uniform. It takes time to organize men and distribute doctors properly, and we must remember that in days of peace the reserve force was not fully equipped with men; so that when war started it was necessary to use doctors first as doctors and not as specialists. We have a war to win, and each of us has a part to play. We are expected to have a working knowledge of general medicine and to contribute this. Our specialty qualifications are a secondary consideration.

Military medicine has three chief purposes: (1) the selection of the physically fit, (2) prophylaxis and (3) the treatment of the injured and sick. While very important, the last is the easiest and the least important in war. The selection and separation from the service of the physically unfit, the malingerers and the psychopathic persons is essential in the formation of a strong man power. These persons should be, and many are, eliminated by the local draft boards, and some more are culled at the induction centers. Yet a number of undesirables get into the service. They are encumbrances and the military forces have no place for them. The Army and Navy are not rendezvous for criminals and men with dementia precox; they are not vacation adventures in which to place problem children, and they have more serious duties than to pamper mollycoddles. We are not fighting inferior races but armies composed of superior specimens of physical manhood. It is to be hoped that we will have enough strong, virile men.

Certainly every cooperation should be given by the medical profession in this matter of selection of the physically fit for our military forces. It is appalling to contemplate the number of inferior specimens of American manhood who have been turned down on entrance or have been separated from the service after induction into the Army. This reflects on our euthenics, our eugenics, our soft ways of living; but that is not the country's problem now. We must first be concerned with removing hell from earth before trying to build a utopia on it.

Preventive medicine has its most important field in wartime. Sanitation, control of vectors, pure food and water, eradication of disease carriers, and immunization are essential medical practices which are second nature to all physicians whether public health experts or dermatologists.

The dermatologist's training fits him for general medicine. It embraces syphilology, histopathology, pharmacology, biochemistry and radiation and physical therapy. He has delved into psychology, gynecology and gastroenterology. Very few realize what a broad field is covered in the examination given by the American Board of Dermatology and Syphilology. The dermatologist's work in allergy gives him a wide perspective on general medicine. It develops an analytic mind which is meticulous about details, searches for truth and protects the dermatologist in a great measure from worshipping therapeutic and etiologic fetishes. Such qualifications bespeak resourcefulness and versatility, which are prime requisites for a medical officer. There are 670 registrants of the American Board of Dermatology and Syphilology. From them will come a valuable addition to the armed forces.

### DERMATOLOGIC PROBLEMS

The variety of dermatoses encountered in military medicine is less than in civilian life because the preliminary examinations cull out many of the chronic conditions such as extensive nevi, neoplasms, lupus

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erythematosus and psoriasis. Atopic dermatitis will be encountered occasionally, but such a diagnosis is a cause for discharge, and therefore the treatment of it is limited. Conditions of a recurrent nature that require repeated hospitalization cannot be tolerated, because every effort of military medicine is aimed at reducing the number of noneffective soldiers. Therefore the chief dermatologic problems will be acute conditions, such as irritations, burns and infections. Medical officers will be spread thinly in most places, and this will require standardization of treatment methods.

The chief dermatologic problems will be therapy, syphilis, insect bites, dermatitis venenata (ivy) and trichophytosis, excepting endemic diseases in foreign countries. The following discussion of these topics contains nothing new to dermatologists but is offered with the purpose of answering questions that are frequently propounded by nondermatologist medical officers who are called on to treat those conditions.

## DERMATOPHYTOSIS

The two chief fungous infections that affect soldiers most commonly are dermatophytosis of the feet and tinea versicolor. They find cultural conditions most favorable. When it is realized that their spores may lurk in the clothing,[1] that sterilization of floors is difficult and that shoes serve as a good culture medium,[2] this increased incidence is explained. The effect of close contact on the incidence of dermatophytosis of the feet is seen in a study of students at the University of California.[3] The incidence of 51.5 per cent at the beginning of a semester increased to 78.6 per cent at the end of the semester in a group of 1,000 freshmen who were exposed to the gymnasium environment.

The successful eradication of pityriasis versicolor entails prevention of the reimplantation of the organism on the skin from the clothing along with persistent local treatment, which in most cases would require individualized care—a desideratum difficult to obtain in a unit that is mobile.

These diseases gain incidence in hot weather, and this is explainable by the fact that heat and moisture favor the propagation of the organisms. Tinea versicolor frequently takes on an erythematous appearance, losing its common fawn colored characteristic. This is no doubt due to the irritation of perspiration and friction of clothing which changes the otherwise inert infection into a mild inflammation. It never loses the characteristic crinkled appearance of the surface epithelium which peels easily on light scraping with an instrument. The condition is commonly seen exhibiting confluent patterns that cover solidly the back or front of the torso. In these widespread cases there are no associated sensory changes—no itching—but an occasional complaint of burning on perspiration.

The effect of heat and perspiration on dermatophytosis of the feet is to raise the incidence of the inflammatory types. Lewis [4] in a cultural study of 215 cases found that Trichophyton gypseum is the organism usually responsible for the inflammatory types of the infection. However, in hot weather other factors enter into the production of disabling foot infections. The presence of the mycelium of the fungus in the rete causes an easy detachment of the protective keratin layer. The high top shoe adds to a cause for perspiration, which in itself macerates the keratin layer. Friction against the shoe and weight bearing add enough trauma to devitalize the skin, which favors the propagation of pyogenic organisms, which thus frequently become the predominant infection.

*Treatment.*—The treatment of infections of the foot is most satisfactorily accomplished by more attention to certain principles of treatment and less to any particular medicament.[5] These demand treatment of the skin rather than of the primary disease. These principles are roughly as follows: 1. Allaying the inflammation before resorting to the stronger fungicides; in other words, not irritating an already inflamed skin with strong chemicals. 2. Rest—the response to treatment is greatly accelerated by avoidance of weight bearing and rubbing of the infected skin. In cases in which there has been an exfoliation of the skin as a result of the disease plus keratolytic medication, the feet should be given time to regenerate a tough integument before the individual resumes heavy duty on his feet. 3. Use of keratolytic agents when the skin is ready for them. Most fungicides serve a dual purpose: first, they have either a fungicidal or a fungistatic effect and, second, they thin the infection by causing a "growing off" of it. 4. Prevention of early recurrences by sterilization of shoes and use of foot powders.

Numerous methods of treatment have been proposed. Strickler [6] has recommended the use of the Henal vacuum vaporizer in using iodine. Swartz [7] has recommended treatment by inhalations of ethyl iodide. (This is not without danger.) Iontophoresis of copper sulfate was advanced as a treatment.[8] This resulted in a short lived wave of popularity and received proof of its worthlessness by the experiments of Greenwood and Rockwood.[9] Various studies on fungistatic and fungicidal properties of drugs have been made but the most significant are as follows: "Iodine transcends all other medicaments in restraining the growth of certain molds";[10] "iodine and chlorine (surgical solution of chlorinated soda) have the highest phenol coefficients";[11] "potassium iodide appears to possess the property of enhancing fungicidal power of vaporized iodine to a considerable degree":[6] the combination of salicylic and benzoic acids works far better than either one alone.[12] The use of iodine is not as popular as Whitfield's ointment or even as the combination in Strickler's solution (which is iodine crystals 1.3 Gm., potassium iodide 1.9 Gm., salicylic acid 1.9 Gm., boric

1. Farley, D. L.: The Viability of Ringworm Fungi in Dry Cutaneous Material, Arch. Dermat. & Syph. **3**: 759 (June) 1921.

2. Ayres, Samuel, Jr.; Anderson, N. P., and Youngblood, Esther M.: Fumigation as an Aid in Control of Superficial Fungous Infections, Arch. Dermat. & Syph. **24**: 283 (Aug.) 1931.

3. Legge, R. T.; Bonar, Lee, and Templeton, H. J.: Epidermomycosis at University of California, Arch. Dermat. & Syph. **27**: 12 (Jan.) 1933.

4. Lewis, G. M., and Hooper, M. E.: Introduction to Medical Mycology, Chicago, Year Book Publishers, 1939, p. 85.

5. Symposium on Practical Management of Eczematous Ringworm of the Hands and Feet, (Athlete's Foot and Dermatophytosis and Dermatophytid), J. Invest. Dermat. **3**: 523 (Dec.) 1940.

6. Strickler, Albert: Fungicidal Properties of Certain Clinically Recognized Fungicides: Laboratory Determination Using the Strickler-Borneman Apparatus and the Henal Vacuum Vaporizer, Arch. Dermat. & Syph. **28**: 836 (Dec.) 1933; The Henal Vacuum Vaporizer, ibid. **25**: 1097 (June) 1932.

7. Swartz, J. H.: Treatment of Fungous Infections with Ethyl Iodide Inhalations: A Review, Arch. Dermat. & Syph. **40**: 962 (Dec.) 1939; Inhalations of Ethyl Iodide in Fungous Infections, ibid. **32**: 551 (Oct.) 1935.

8. Haggard, H. W.; Strauss, M. J., and Greenberg, L. A.: Fungous Infections of Hands and Feet Treated by Iontophoresis of Copper, J. A. M. A. **112**: 1229 (April 1) 1939.

9. Greenwood, A. M., and Rockwood, Ethel M.: Iontophoresis of Copper Sulfate in Cases of Proved Mycotic Infection, Arch. Dermat. & Syph. **44**: 800 (Nov.) 1941.

10. Schamberg, J. F., and Kolmer, J. A.: Studies in the Chemotherapy of Fungous Infections: the Fungistatic and Fungicidal Activity of Various Dyes and Medicaments, Arch. Dermat. & Syph. **6**: 746 (Dec.) 1922.

11. Emmons, C. W.: Fungicidal Action of Some Common Disinfectants on Two Common Dermatophytes, Arch. Dermat. & Syph. **28**: 15 (July) 1933.

12. Gould, A. G., and Carter, Edna K.: Fungistasis in Ringworm of the Toes and of the Feet, Arch. Dermat. & Syph. **22**: 225 (Aug.) 1930. Sharlit, Herman, and Muskatblit, Emanuel: A Search for a New Method for the Determination of the Fungicidal Action of Chemicals, ibid. **25**: 615 (April) 1932.

acid 3.8 Gm. and alcohol [50 per cent] to make 59.1 cc.). This is partly because of the frequent irritation of the skin induced by iodine. However, a recent product, iodocholeate,[13] gives promise of becoming a valuable addition to the armamentarium of "ringworm therapeutics" because (1) the iodine in iodocholeate is released from its adsorption to bile salts as free iodine more slowly than the iodine in the tincture—in other words, is less volatile; (2) the iodine in this product combines less with protein than the iodine of the tincture. Schamberg and Kolmer[10] found brilliant green the best restrainer of growth and methylrosaniline the best fungicide among the dyes. Castellani's formula[14] of carbolfuchsin, though it does not serve as a panacea, serves a good purpose in practice, particularly when a nonirritating fungistatic agent is desired. Wise and Wolf[15] listed the following agents as fungistatic or fungicidal and suitable for use in practice: ammoniated mercury, peruvian balsam, benzoic acid, betanaphthol, mercury bichloride, iodine, chrysarobin, oil of cinnamon, phenol, potassium permanganate, pyrogallol, resorcinol, salicylic acid, silver nitrate, sodium thiosulfate, sulfur, tar, thymol.

In treating the disease in the Army one cannot always follow a fixed routine and has to vary treatment according to conditions as well as what medicaments are obtainable. The following routine is suggested, as it employs drugs that are standard items on the Army drug list. It can be divided roughly into (1) treatment in the acute inflammatory stage, (2) treatment in the subacute stage, (3) treatment to the intact skin with fungicidal agents.

Treatment for Acute Inflammation: Rest is a valuable aid, particularly if the secondary infection has resulted in cellulitis or lymphangitis. If the secondary pyoderma is attended with pustules, drainage is essential. Tops of all pustules should be manicured away and wet dressings should be used. It is important in this stage not to use eczematogenic drugs (i. e. those likely to cause a sensitization dermatitis, such as picric acid). Neither should keratolytic agents be used, such as the Whitfield formula. The condition should be treated for what it is—a cellulitis. Wet dressings continuously applied are best. The choice of the agent is optional. One of the following will be of value: (1) liquor aluminum acetate diluted 10 per cent, applied at room temperature, uncovered to allow evaporation; (2) warm potassium permanganate solution (1:6,000); (3) warm boric acid solution; (4) warm magnesium sulfate solution. The dressing should be taken off daily. It is helpful to soak the affected parts in warm soapsuds for ten to fifteen minutes to soften the skin. At this time all pustules and attached skin that dams back infection should be carefully manicured away. This is to be followed by some oxidizer such as a 2 per cent solution of sodium perborate for another ten to fifteen minutes. It is an additional aid in softening the detritus and epidermal scales. The wet pack is reapplied for another twenty-four hours. In using the wet pack one must take care to see that it is applied correctly. Otherwise time will be lost. It should be applied so that the dressing is solidly against every contour of the inflamed skin; to accomplish this pledgets should be placed between the toes and the bandage should bring the dressing up against the skin, for example a dressing applied to the instep. After a few days the acute inflammation subsides, the drainage stops and there is visible evidence of epithelial repair.

Treatment for Subacute Inflammation: Even here the strong fungicides are contraindicated. However, some of the fungistatic agents can be used, such as carbolfuchsin or methylrosaniline. A suitable formula for this is McFarland's[16] (methylrosaniline 6 Gm., alcohol 24 cc. and water 120 cc). The epidermis is not tough. In fact there may yet be denuded areas. The soaks can be continued each day and followed by a dressing with a mild antiseptic ointment, such as boric acid, ammoniated mercury, or the methylrosaniline, followed (after it dries) with simple Lassar's paste and a dressing.

Active Fungicidal Treatment: When the skin repairs a change to active fungicidal agents can be considered. The most popular and the one that is most serviceable is Whitfield's formula. All strong ointments that are applied to the feet are preferably applied at night, particularly if it happens to be one containing an essential oil or a substance that is apt to act as a vesicant when the shoes are worn. If the change is made to Whitfield's ointment when the skin is tender, a 50 per cent strength had best be used. A modification of this formula put in liquid form is advantageous for a person who naturally has hyperhidrosis, as it has a drying action and thus inhibits propagation of the fungus. Peck and his associates[17] have shown that some of the organic acids naturally present in the skin act as fungistatics, and this is an indication for incorporating into the prescription one of these, such as lactic acid. I feel that it fortifies the efficacy of the combination of salicylic and benzoic acids in a liquid menstruum.

Foot Powders: The use of foot powders is of distinct value and they are recommended. They aid in keeping the feet dry. That is one advantage. Another is that if they contain a fungicidal or fungistatic agent a better opportunity is presented for a more continuous application, as perspiration dissolves the medicine. In the shoes they help to weed out the source of reinfection. A serviceable foot powder is the following: thymol 1 per cent, boric acid 10 per cent, zinc oxide 20 per cent, purified talc to make 100 per cent. The use of foot powders containing as much as 3 per cent salicylic acid is contraindicated for soldiers because the salicylic acid adds to the macerating effect of the perspiration and causes a denudation of the epithelium. Thus, it may defeat its purpose in the attempt to prevent a crippling effect of the infection.

Irradiation: Roentgen treatments are of distinct value in the inflammatory types of the infection and in the subacute types. They have an antipruritic effect probably faster than any other agent and also a satisfactory sedative effect on inflammation. In fact, roentgen treatments contribute greatly in reducing the duration of the inflammatory stage of the infection. They should be administered in small doses (70 roentgens) at weekly intervals. Larger doses do no more good, nor will oft repeated treatments do any more than weekly treatments. Usually not more than three or four are necessary in the worst cases, and rarely are that many

13. Lever, W. F.: Iodocholeate, a New Fungicidal Preparation: Preliminary Report, Arch. Dermat. & Syph. **40:** 19 (July) 1939.
14. Castellani, Aldo: Treatment of Certain Types of Epidermophytosis by Means of a Carbol-Fuchsin Paint, New Orleans M. & S. J. **80:** 833 (June) 1928.
15. Wise, Fred, and Wolf, Jack: Use of the Dermal Parasiticides, J. A. M. A. **107:** 1126 (Oct. 3) 1936.
16. McFarland, A. R.: The Use of Gentian Violet Locally in Dermatologic Conditions, Arch. Dermat. & Syph. **17:** 16 (Jan.) 1928.
17. Peck, S. M.; Rosenfeld, Herbert; Leifer, William, and Bierman, William: Role of Sweat as a Fungicide: With Special Reference to Use of Constituents of Sweat in the Therapy of Fungous Infections, Arch. Dermat. & Syph. **39:** 126 (Jan.) 1939. Peck, S. M., and Rosenfeld, Herbert: The Effects of H/Ion Concentration, Fatty Acids and Vitamin C on Growth of Fungi, J. Invest. Dermat. **1:** 237 (Aug.) 1938.

necessary provided judicious local care is given. Using roentgen rays with such a plan keeps the dosage well within safety limits. Many have the mistaken idea that roentgen rays are fungicidal and bactericidal. This is not the case. Jacobson [18] experimented with effects of them on cultures of various fungi and concluded that "the results of this investigation, while not conclusive, seem to suggest that the beneficial therapeutic effects of roentgen irradiation on the clinical mycoses are largely due to the action of these rays on the tissues primarily, which, in turn, probably through some intermediary unknown factors of immunity generated in them by the roentgen rays, exercise an adverse effect on the infecting parasites in situ." Ultraviolet radiation itself has no curative value. However, it activates the dyes and with them is of therapeutic benefit.[19]

Trichophytin: The use of trichophytin as a therapeutic agent is not yet on a well established basis. Its use as a diagnostic agent, particularly in the handling of vesicular dermatitis of the fingers, is unquestionable. Recent work on the preparation of it may add somewhat to its therapeutic efficacy as an immunizing agent. Peck and his associates [20] have revived the idea that there is a skin reactive factor and an immunizing factor in trichophytin, and they were able to produce either by controlling the $p_H$ of the culture medium. Miller's [21] method of preparation yielded a trichophytin which stimulated the production of complement fixing antibodies and precipitins when injected into rabbits, and he stated that it was suitable for use in serologic tests to detect the presence of circulating antibodies in human infections. It is beyond the pale of human imagination to expect that ringworm vaccine will ever replace the need for local medication of the infection.

Prophylaxis: Infected nails often serve as a source of reinfection and should receive attention. Avulsion is sometimes recommended though not always necessary. By persistent care and attention, scraping and macerating the infected nail substance and application of one of the commonly used medicaments, it is the usual experience for one to grow off the infected nail. This cannot be accomplished in one whose nails do not grow at a normal rate.

A source of infection in civil life is commonly floors; except in fixed barracks this is not an important source in the Army. The soldier's shoes are his greatest source of reinfection. Many is the time that his shoes do not have time to dry or get an inside cleaning. However, every attempt should be made to sterilize them, according to the opportunity. Formaldehyde is the most efficacious and cheapest.[22] Much of the crippling effects of fungous diseases of the feet can be prevented by sterilization of the shoes and socks, keeping the feet as dry as possible, the use of a foot powder and early treatment of latent infections before the hot season commences.

Of all cutaneous diseases of soldiers, trichophytosis is the most important because of its potentiality of taking him off of his feet.

### DERMATITIS VENENATA (POISON IVY AND TROPICAL PLANTS)

No better opportunity can be offered for studies on the treatment and prophylaxis of poison ivy dermatitis than the Army on maneuvers. Shelmire [23] and Stratton [24] have indicated that the antigenic principle is the same regardless of the plant (one or more species of which is widespread over the United States). The former has shown by experiments how difficult it is to wash the active principle off of the hands or clothing. The soldier in the field has little opportunity to avoid spreading it over himself by his clothes or other fomites, which accounts for many cases of severe crippling dermatitis. His contact, when it occurs, is usually not a light one. On maneuvers frequently he has to crawl or lie down in the plant, and the practice of camouflage does not permit any selection of leaves in which to hide himself, cannon or truck. The plant vies with gas in producing noneffectives in certain locations.

*Treatment.*—Regardless of the severity of the dermatitis, it is incapacitating to a large percentage of soldiers. The problem is a dual one—treatment and prophylaxis. Patients with severe involvement require hospitalization. Such persons need a complete change of clothing and environment to prevent further inoculations of their skin with the irritant. There are a long list of prescriptions and medicines advised. Calamine lotion is the universal agent used. It is palliative in cases of mild involvement. The ones with a considerable amount of vesicles and bullae require wet packs, and the standard preparations are Burow's, boric acid and potassium permanganate solutions. Subacute irritations are frequently handled satisfactorily by painting with saturated solution of potassium permanganate. It, Castellani's formula of carbolfuchsin and boric acid have antipruritic qualities. A boric acid paste is a good antipruritic. Cold is better than heat in that respect. The selection of the drug used depends a great deal on what is most readily obtainable. In this respect potassium permanganate is the most practical because it is cheap and requires no great amount of room in a medicine kit. Determination of the practicability of sodium perborate ointment [25] as a protective for soldiers needs further study. The probability of its deterioration and the bulkiness of jars of it do seem to rule against its adoption.

The value of injections of the extract of the plant for treatment as well as for prophylaxis is still in a state of flux. Reports on their efficacy are contradictory. Zisserman and Birch [26] studied a group of 1,731 boys at a boy scout camp. Three hundred and four received prophylactic intramuscular injections. The incidence of subsequent poison ivy dermatitis was 51.6 per cent in the treated group and only 33.6 per cent in the camp as a whole. Greenberg and Mallozzi [27] studied a group and found that 27 per cent who were specifically "immunized" contracted poison ivy dermatitis, while it occurred in 36 per cent of those who received control injections. A list of other contributors to the subject

18. Jacobson, H. P.: Effects of Roentgen Rays on Fungi in Vitro, Arch. Dermat. & Syph. **38**: 38 (July) 1938.

19. Gomez-Vega, Paulina: Effect of Irradiation and Irradiation plus Sensitization on Yeastlike Fungi and Related Organisms, Arch. Dermat. & Syph. **34**: 961 (Dec.) 1936.

20. Peck, S. M.; Glick, Arthur, and Weissbard, Edward: Trichophytin: II. The Apparent Separation of the Skin Reactive Factor from the Therapeutic Principle in Trichophytin, Arch. Dermat. & Syph. **44**: 816 (Nov.) 1941.

21. Miller, H. E.; Stewart R. A., and Kimura, Frances: Undenatured Trichophytin: Preparation and Clinical Application, Arch. Dermat. & Syph. **44**: 804 (Nov.) 1941.

22. Henderson, Yandell: Fungous Infection of the Feet: Fumigation of Shoes with Formaldehyde as a Mean of Treatment, Arch. Dermat. & Syph. **26**: 710 (Oct.) 1932. Ayers, Anderson and Youngblood.[2]

23. Shelmire, Bedford, The Poison Ivy Plant and Its Oleoresin, J. Invest. Dermat. **4**: 337 (Oct.) 1941.

24. Stratton, E. K.: Poison Oak and Poison Ivy: I. Dermatitant Units as Standard Measure of Potency for Extracts from these Plants, J. Allergy **11**: 591 (Sept.) 1940.

25. Schwartz, Louis; Warren, L. H., and Goldman, F. H.: Protective Ointment for the Prevention of Poison Ivy Dermatitis, Pub. Health Rep. **55**: 1327 (July 26) 1940.

26. Zisserman, L., and Birch, L.: The Prophylaxis of Poison Ivy Dermatitis with an Extract of Rhus Toxicodendron, J. Allergy **10**: 596 (Sept.) 1939.

27. Greenberg, Solomon, and Mallozzi, Ella D.: Experiments in Poison Ivy Sensitivity: Effects of Specific Injections on the Level of Sensitivity to Quantitative Patch Tests and on Clinical Susceptibility, Arch. Dermat. & Syph. **42**: 290 (Aug.) 1940.

who report good [28] and poor or no [29] results is appended. It is seen that the ones who give encouraging support to the idea that immunizing results can be obtained are Shelmire, Molitch and Poliakoff, and Keeney. Shelmire gave orally ascending doses of a 1:25 or 1:10 dilution of the oleoresin for a period of several months, and he demonstrated varying degrees of reduced sensitivity. The technic that Molitch and Poliakoff used consisted in continuous injections from the first appearance of the poison ivy leaves until the first frost, a period of five months: the dosage was that recommended by Spain and Cooke [30] at intervals of a week. The first dose was 1 cc. of a dilution of 1:10,000, with gradual increase in the strength up to 1 cc. of 1:500. Keeney [28] recommends protection by taking advantage of the refractory period (six to eight weeks) that follows a positive patch test. Further work is necessary to standardize this procedure. For protecting soldiers in the field it offers the advantage of simplicity and the saving of supplies and administrative details.

Stratton [24] has recommended a standardization of dosage of the extract on the basis of the dermatitis producing activity of an extract on the shaved skin of an animal. He has selected as "representing 10,000 dermatitant units that quantiy of poison oak or poison ivy extract contained in 0.1 cc. of designated solvents, which, when applied 'without cover' to the epilated skin of animals which do not become sensitized, such as the rabbit, rat or mouse, in the form of a stripe (3 cm. in length by 6 m. in width) is just sufficient to elicit an erythematous reaction within forty-eight hours." There is need for a standardization of poison ivy extracts. It has been shown by more than one observer that products of the commercial houses vary in their strengths.

Many physicians use one or more of the products in treatment or in an attempt to immunize. Many patients demand it. An occasional dramatic improvement in signs and symptoms is seen, and for this reason, if no other, its popularity will continue. A conclusion should not be drawn regarding immunization unless it is definitely known that the individual actually has had a "clinical exposure." There is still a need for further work to determine what is the best method of hyposensitization to protect a sensitive person from incapacitating attacks of the dermatitis when exposed in an ordinary manner. A plan that is practical would be a valuable contribution to military medicine.

### TROPICAL PLANTS

In the tropics there are plants which cause irritation of the skin either by hairs, thorns or spines or by their irritating sap. They are listed [31] in the accompanying tabulation.

### DERMATITIS DUE TO INSECTS

Satisfactory methods of curbing some of the insects have been worked out by military medicine in the past, notably those for pediculosis corporis. The delousing methods used in the last war may again be necessary, but up to date this has not become much of a medical problem.

*Tropical Plants Causing Irritation of the Skin*

| Plant | Irritating Principle |
|---|---|
| Spanish nettle (shrub) | Stinging hairs on stems |
| Cow itch (vine) | Hairs on seed pods |
| Panama (tree) | Hairs of fruit |
| Acacia (shrub) | Ants in its spines |
| Black palm | Spines of leaf and trunk |
| Beach apple | Sap |
| Mango | Sap |
| In the Philippines | |
| Kaong palm | Hairs on fruit |
| Dumayaka palm | Hairs on fruit |
| Fishtail palm | Hairs on fruit |
| Lipang-kalabao (tree) | Hairs on leaves |
| Lipang-morado (tree) | Hairs on leaves and stems |
| Lipa (tree) | Hairs on trunk or leaves |
| Dilano (vine) | Hairs on leaves and stems |
| Pungapung (shrub) | Juice of stem |
| Ligas (tree or shrub) | Sap of trunk |
| Buta-buta (tree) | Latex of bark (a violent irritant—poisonous if taken internally |
| Panay | |
| Kamanday (tree) | Sap of trunk (fatal if taken internally) |
| Dalit (tree) | Sap is poisonous internally |

Scabies is ever present, but its incidence is held down to an inappreciable amount by the monthly physical examinations and isolation practices. Yet when troops are in the field more favorable conditions for its increase arise. Its diagnosis is not difficult except in atypical cases, and in them a trained dermatologist can render aid.

There are two insects which in southern United States are particularly voracious and cause no end of trouble in the hot season—chiggers and ticks. Any one who has not had the experience of a generalized infestation of chiggers over his body has not yet tasted one of life's bitterest pills. They give rise to pruritic papules which itch long after the insect has been destroyed. They and the tick bites are the beginning of many cases of pyoderma, which result in a further loss of troops because of hospitalization. The impetiginous and furuncular lesions of tick bites frequently result in small nodular granulomas which involute very slowly and which in some cases undergo exacerbations of itching days or weeks apart. In some instances a cycle of neurodermatitis develops. During the maneuvers of the fall of 1941 there were no patients with Rocky Mountain spotted fever and only 1 with tularemia evacuated from the field to the Station Hospital at Fort Sam Houston. This hospital did not receive any patients evacuated from any Pacific states. How-

28. Reports of good results include:
Williams, C. F.: Ivy Poisoning, M. J. & Rec. (supp.) **119:** 131 (June 4) 1924.
Alderson, H. E.: Treatment of Poison Oak Dermatitis, California & West. Med. **23:** 982 (Aug.) 1925.
Bivings, G. L.: Successful Desensitization and Treatment of Poison Ivy and Poison Oak Poisoning, Arch. Dermat. & Syph. **9:** 602 (May) 1924.
Gowen, G. H.: Treatment and Prevention of Rhus Toxicodendron Poisoning, J. Allergy **4:** 519 (Sept.) 1933.
Caulfield, A. H. W.: Prevention of Poison Ivy Dermatitis by the Intramuscular Injection of "Rholigen," Canad. M. A. J. **37:** 18 (July) 1937; Specific Diagnosis and Treatment of Poison Ivy (Rhus Tox) Dermatitis, J. Allergy **9:** 535 (Sept.) 1938.
Attix, J. C., and Rommell, J. C.: The Treatment and Prevention of Ivy Poisoning, Clin Med. & Surg. **46:** 410 (Oct.) 1939.
Foerster, H. A.: The Treatment of Poison Ivy, J. Oklahoma M. A. **31:** 245 (July) 1938.
Sharlit, Herman, and Newman, B. A.: Specific Treatment in Rhus Dermatitis, New York State J. Med. **37:** 61 (Jan. 1) 1937.
Molitch, Matthew, and Poliakoff, Samuel: Prevention of Dermatitis Venenata Due to Poison Ivy in Children, Arch. Dermat. & Syph. **33:** 725 (April) 1936; Further Report, ibid. **36:** 1086 (Nov.) 1937.
Strickler, Albert: Treatment of Dermatitis Venenata, J. Cutan. Dis. **36:** 327 (June) 1918; The Toxin Treatment of Dermatitis Venenata, J. A. M. A. **77:** 910 (Sept. 17) 1921; The Value of the Toxin (Antigen) of Rhus Toxicodendron and Rhus Venenata, ibid. **80:** 588 (June 2) 1925.
Schamberg, J. F.: Desensitization of Persons Against Poison Ivy, ibid. **73:** 1213 (Oct. 18) 1919.
Keeney, E. L.: Studies on Human Hypersensitivity to Poison Ivy, South. M. J. **35:** 408 (April) 1942.
Shelmire, Bedford: Hyposensitization to Poison Ivy, Arch. Dermat. & Syph. **44:** 983 (Dec.) 1941.

29. Reports of poor or no results include:
Bachman, L. O.: Prophylaxis of Poison Ivy: Use of an Almond Extract in Children, J. Pediat. **12:** 31 (Jan.) 1938.
Krause, G. L., and Weidman, F. D.: Ivy Poisoning, J. A. M. A. **84:** 1996 (July 27) 1925.
Templeton, H. J.: Untoward Reactions Following Toxin Treatment for Dermatitis Venenata, Arch. Dermat. & Syph. **20:** 83 (July) 1929.
Corson, E. F.: The Value of the Toxin of Rhus Toxicodendron and Rhus Venenata, J. A. M. A. **81:** 59 (July 7) 1923.
Simon, F. A., and Lotspeich, E.: Observations on Sensitivity to Poison Ivy Dermatitis, J. Invest. Dermat. **2:** 143 (June) 1939.

30. Spain, W. C., and Cooke, R. A.: Studies in Specific Hypertensitiveness: XXVII. Dermatitis Venenata. Observation on the Use of a Modified Extract from Toxicodendron Radicans (L.), J. Immunol. **13:** 93 (Feb.) 1927.

31. Infantry J., April 1942, p. 49.

ever, in the future, because of the interchange of troops and the rapid transport of them, the spread of diseases ordinarily endemic in certain localities can be expected. The curbing of chigger and tick bites can be accomplished in peace time by burning undergrowth and ground. It will not be done in wartime because of the need of cover. Ticks can be eradicated from the body by picking, but not so the little chigger, which cannot be seen even with a lens until he changes his color with engorged red blood cells. A favorite night pastime of soldiers in the field is to pick ticks off of one another. I was told that commonly when a marching column halted last summer every one from the general on down took off his shirt and started picking himself and his clothes. Such a method of eradication is a crude way of protection, and medicine should provide a better one. It should be emphasized that protective local applications should not be too bulky and should be easily applied. The application of sulfur and derris root powder is helpful. Application of kerosene or pyrethrum oil to the insect when he has attached himself, followed by bathing, is efficacious.

The control of the spread of leishmaniasis, yaws, verruga peruana as well as the insect borne fevers can be aided by the use of insect repellents.

### SYPHILIS

Syphilis is handled in the Army by the urologic service, which is a division of the surgical service. Formerly dermatology was a part of the urologic service. In hospitals where dermatology is under the medical service, syphilology thus is not a part of dermatology. The opportunity for a dermatologist to do any work on syphilis will depend on the situation, such as the size of the hospital. The incidence of it among inductees is not known and cannot be stated exactly until mobilization is complete. An early report from the Texas State Headquarters for Selective Service in June 1941 showed 2.17 per cent of 3,626 rejections because of the disease. The incidence has been found higher among inductees generally (4.2 per cent). "The admission rate for all venereal diseases for the whole army was 42.5 per thousand strength in 1940 as compared to 29.6 in 1939, an increase of 44 per cent. Eighteen per cent of the cases were syphilis and 72 per cent were gonorrhea. The percentage due to syphilis was slightly lower and that due to gonorrhea slightly higher than has been usual in the past years. The percentage due to chancroid and lymphogranuloma venereum shows little change from 1939." [32]

All patients with the condition in an early stage are hospitalized until the condition becomes noninfectious. The syphilitic register of the Army is very successful and is the ideal method of handling the infected in a manner which will stamp out the disease. The soldier's record of syphilis follows him wherever he goes; it contains his record of treatment, collaborated laboratory tests, pertinent clinical data from the beginning to the time of cure or when the case is closed. Treatment for early syphilis is standardized so that the optimum requires continuous treatment with alternating courses of thirty each of arsphenamine and bismuth injections for one year, with clearance only after the serologic reactions of blood and spinal fluid have become and remain negative for a year. On completion of the optimum treatment the patient is followed up at frequent intervals. Careful physical examination is made after approximately six months and at the end of the year. The final examination includes an examination of the heart and great vessels.

The technic of massive dose arsenotherapy of early syphilis by the intravenous drip method has not been adopted by the Army. It has promise of its most successful application in the fixed hospitals of the Army because the soldier with syphilis is hospitalized during his infectious period anyway. He could receive his full course of arsenicals during this period. Whether or not this was pursued with follow-up courses of bismuth, the total time lost from service as a result of treatment would be considerably less with this plan of treatment. It also offers savings in the administrative costs of handling the case. The untoward effects such as toxicodermas, liver or kidney damage, encephalitis, neuritis, blood dyscrasias and nitritoid reactions are contrary to what was at first expected—surprisingly mild or nil. The fatalities from the treatment in Leifer, Chargin and Hyman's [33] series was one death among 382 cases (0.25 per cent), and five deaths (0.3 per cent) among 1,600 cases reported by Elliott and the U. S. Public Health Group.[34] It gives promise of curing 83 per cent. If current expectations from the studies hold up, it may become a standard procedure for all clinics. However, it is still considered to be in the experimental stage and is not adopted by the Army.

### DERMATOLOGIC THERAPY

The treatment of dermatologic conditions in the Army is distinctly different than in civil life. It will be variable, dependent on whether in the field or in the hospital and the size and location of the hospital. In the smaller dispensaries treatment necessarily has to be simple, and if it is not effective the patient has to be evacuated to a station or general hospital. The dermatologic work is placed as a separate section under the medical service in hospitals large enough to make a special service practicable. Dermatologic therapy calls for resourcefulness, as the dermatologist will not find every convenience and modality to which he has become accustomed in his civilian practice. His allergy studies will be handled by another department and his radiation therapy will be delegated to still another department. His local applications will depend on what is a standard drug for the Army. He will have to plan his technic of treatment based on general principles (such as reducing agents and soothing agents available).

The chief difficulty will be the choice of a proper base. What is an ideal base is not generally agreed on; however, it is generally agreed that bases containing emulsifying agents make more effective ointments.[35] The selection of it would depend on what is available. It should be as simple as possible and not require much time in processing. I have used a base containing 5 per cent Duponol in hydrous wool fat and petrolatum and have demonstrated its repeatedly increased efficiency over plain petrolatum, with no sensitivity to it. Another suggested one is diglycol stearate 10 per cent, white wax 3 per cent, cetyl alcohol 3 per cent, petrolatum 4 per cent, glycerin 4 per cent and water 100 per

32. Report of the Surgeon General, U. S. Army, to the Secretary of War, 1941, p. 41.

33. Leifer, William; Chargin, Louis, and Hyman, H. T.: Massive Dose Arsenotherapy of Early Syphilis by Intravenous Drip Method: Recapitulation of the Data—1933 to 1941, J. A. M. A. **117**: 1154 (Oct. 4) 1941.

34. Elliott, D. C.; Baehr, George; Shaffer, L. W.; Usher, G. S., and Lough, S. A.: An Evaluation of the Massive Dose Therapy of Early Syphilis, J. A. M. A. **117**: 1160 (Oct. 4) 1941.

35. Maynard, M. T.: Triethanolamine, an Adjunct to Dermatology, Arch. Dermat. & Syph. **25**: 1041 (June) 1932. Goodman, Herman: Cosmetic Dermatology, ibid. **36**: 116 (July) 1937. Fantus, Bernard: Choice of Ointment Vehicles, J. A. M. A. **107**: 861 (Sept. 12) 1936. Duemling, W. W.: Wetting Agents: New Synthetics of Use in Finer and More Efficient Topical Dermatologic Therapy, Arch. Dermat. & Syph. **43**: 264 (Feb.) 1941.

cent. It costs little more than plain petrolatum. Recently 50 cases were subjected to make patch tests with this base without a reaction. If one wants a greaseless base or cream, the formula of Remington [36] is suitable. It contains only one drug that is not standard on the Army drug list, namely stearic acid. Diglycol stearate mixed with water to suitable consistency also serves as a greaseless cream. One pound (450 Gm.) of it will make 10 pounds (4,500 Gm.) of base (cost $1).

Dependent on the volume of cases, the technic of treatments will vary. If large groups of men have to be handled in a short length of time the treatment may have to be given in a wholesale manner.

Whatever methods are adopted, the prime motive cannot be lost, and that is to dispose of the patient as expeditiously as possible—either back to duty or to a place where he will not interfere with the efficiency and mobility of the military machine. If his condition is one that is recurrent and necessitates frequent hospitalization (i. e. atopic dermatitis, or dermatitis herpetiformis), the Army has no use for him. Cases falling into this category require discharge from the service.

### RESEARCH

The physician in the Army is constantly faced with research problems. Many times his duties or his location will not allow the prosecution of them. His attention may be taken with administrative problems, little time for study being left. Or in other situations time may hang heavy on him. In either instance, his contributions to medicine will call for a little more effort than in civilian life. Since this is a world war, many will be stationed where there will be opportunities for them to gain first hand knowledge of diseases rare in their homeland. One may be stationed in a leprosy country, another in South America, where he will see chromoblastomycosis. Some may get a wide experience with yaws. Will one see the Aleppo boil as commonly as one does impetigo in this country? And likewise the opportunity of comparing the American form of leishmaniasis? Pinta may be experienced by the New Yorker, and verruga peruana by the Californian. The prospects for a wide experience in medicine for the Army medical officer are limitless and call for an unlimited fund of knowledge.

There is danger of American medicine losing many of its gains as a result of the war. All must strive to keep up the standards of modern achievements. This idea is best expressed by Skinner: [37] "When the sources of learning, science and culture are dried up by war, not only the professors and fellows are lost to progress but the great groups of students in their wakes are lost to the future. War not only grinds future soldiers, citizens and even children in the dust but it createst a dust bowl that future generations must refertilize and cultivate before any scientific spirit and accomplishment can sprout again. Moreover, when frontiers are closed by war there is no longer that comradeship of scientists that provokes useful adventures through the exchange of ideas and of literature. The whole world would halt in what we hope is useful progress if the flame of science were not kept lit somewhere, somehow. Unfortunately, science and culture cannot bivouac for an intellectual rest. Science must be kept nourished by thoughts and ideas that have no place to develop amidst the terrors of warfare. One cannot establish a blackout for science for the duration and then expect it to flourish when the bombing is over. This is especially true in the total war that is now the world's fashion." All other sources of medical knowledge are dammed up, and there is now more than ever the urgent need for America to keep alive the continued interest and progress of scientific medicine. American dermatology has made great strides since the establishment of the Broome Street Infirmary for Diseases of the Skin by H. D. Bulkley and John Watson in 1837.[38] Let us hope that none will be lost and that, despite the handicaps thrust on us by the present war, American dermatology will continue its contributions to medicine. This is a challenge to all—both those in the military service and the ones who are carrying on at home under added burdens.

36. Remington's Practice of Pharmacy, ed. 8, Philadelphia, J. B. Lippincott Company, 1937, p. 1999.

37. Skinner, E. H.: The Philosophical and Practical Aspects of the Economics of Cancer Control: Janeway Lecture, Am. J. Roentgenol. 47:1 (Jan.) 1942.

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## THE INCIDENCE OF NUTRITIONAL AND VITAMIN DEFICIENCY

### A SURVEY OF PATIENTS ENTERING STANFORD UNIVERSITY HOSPITAL

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The importance of adequate nutrition in maintaining the health of the nation has been clearly brought to the fore by the war emergency. But while good nutrition must be implemented and any indifference to this paramount problem must be overcome, it is obviously necessary, in order to work intelligently, that the true needs of the situation be understood as fully as possible. Although many studies have already been published, it is desirable to make even more surveys of vitamin deficiency on different groups of people in various parts of the country so as to be on really solid ground. The present study was carried out to gain information about nutritional deficiency in a certain population group in California.

TABLE 1.—*Relation of Adequacy of Diet to Social Rating and to Clinical Signs of Vitamin Deficiency*

| | | |
|---|---|---|
| Total patients | 385 | (100 %) |
| Total with vitamin deficiency disease | 12 | ( 3.1%) |
| Total with "good" social service rating | 348 | ( 90.4%) |
| Total with "poor" social service rating | 37 | ( 9.6%) |
| Total with "adequate" diet | 297 | ( 77.1%) |
| Total with "inadequate" diet | 88 | ( 22.9%) |
| Social rating good; "adequate" diet | 277 | ( 79.3%) |
| Social rating good; "inadequate" diet | 71 | ( 20.7%) |
| Social rating poor; "adequate" diet | 20 | ( 54.0%) |
| Social rating poor; "inadequate" diet | 17 | ( 46.0%) |
| Adequate diet; deficiency disease | 2 | ( 0.7%) |
| Adequate diet; no deficiency disease | 295 | ( 99.3%) |
| Inadequate diet; deficiency disease | 10 | ( 11.4%) |
| Inadequate diet; no deficiency disease | 78 | ( 88.6%) |

SUMMARY

| | | Adequate Diet | Inadequate Diet |
|---|---|---|---|
| Total patients | 385 (100 %) | 297 (100 %) | 88 (100 %) |
| Total showing clinical vitamin deficiency | 12 ( 3.1%) | 2 ( 0.7%) | 10 ( 11.4%) |

### MATERIAL AND METHODS

The people studied were patients admitted to the adult medical wards of Stanford University Hospital. They were of all ages and represented for the most

38. Pusey, W. A.: The History of Dermatology, Charles C Thomas, Publisher, Springfield, Ill., 1933, p. 135.

From the Department of Medicine, Stanford University School of Medicine.

TABLE 2.—*Vitamin Survey, 1940-1941*

| STATUS | | STATUS | |
|---|---|---|---|
| Name: | Date entered: | Name: | Date entered: |
| Clinic number: | Date dismissed | Clinic number: | Date dismissed |
| Address: | OPD follow-up: | Address: | OPD follow-up: |
| Age: Sex: | | Age: Sex: | |
| Economic status: | | Metabolic defects and increased demands: | |
| Social service rating: | | Hyperthyroidism: | |
| Occupation: | | Myxedema: | |
| Diet: | | Diabetes mellitus: | |
| Dairy products: | | Renal stone: | |
| Citrus fruits: | | Nephritis: | |
| Leafy greens: | | Liver disease (cirrhosis and so on): | |
| Cereals: | | Chronic infectious disease and fever: | |
| Red meats: | | Pregnancy and lactation: | |
| Calories: | | Intravenous dextrose: | |
| Supplements: | | Arteriosclerosis: | |
| Absorption: | | Gout: | |
| Diarrhea: | | Conditions associated with malnutrition: | |
| Vomiting: | | Caloric inadequacy: | |
| Gastrointestinal disease (neoplasm, obstruction, fistula, infections): | | Alcoholism: | |
| | | Psychic disorders: | |
| Jaundice (obstructive): | | Lack of teeth: | |
| Pancreatic disease: | | Miscellaneous: | |
| Achlorhydria and achylia: | | Final diagnosis: | |
| Cathartics (oils and so on): | | Comment (including treatment): | |

TABLE 3.—*Vitamin Deficiency Studies*

| Skin | A | $B_1$ | Ribo-flavin | Nicotinic Acid | $B_6$ | C | D | E | K |
|---|---|---|---|---|---|---|---|---|---|
| Acne and acneform eruptions | X | | | | | | X | | |
| Acrodynia | | X | | X | | | | | |
| Arsenical dermatitis | | | | | | X | | | |
| Athlete's foot | | | | | | X | | | |
| Bruising | | | | | | X | | | X |
| Cheilosis and sore lips | | | X | | | | | | |
| Eczema | | B | | | | | X | | |
| Erosions around eyes | | | X | | | | | | |
| Exfoliative dermatitis | X | | | | | | | | |
| Follicular keratitis | X | | | | | X | | | |
| Herpes zoster | | X | | | | | | | |
| Hyperpigmentation | | | | X | | X | | | |
| Itching and burning | | | | X | | | | | |
| Lupus erythematosus | | | | | | X | | | |
| Nails: trophic disturbance | X | | X | | | | | | |
| Pemphigus | | | X | | | | X | | |
| Pellagra skin lesions | | | | X | | | | | |
| Pruritus: anal and vaginal | | | | | | | | X | |
| Psoriasis | | | X | | | X | X | | |
| Sharkskin nose | | | X | | | | | | |
| Skin dyscrasias: dry, keratosis pilaris | X | | | | | | | | |
| Urticaria | | | | | | X | | | |
| Alimentary Tract | | | | | | | | | |
| Anorexia | X | X | | | | | | X | |
| Constipation and gastrointestinal hypertonicity | | X | | | | | | | |
| Cramps and abdominal pain | | | | X | X | | | | |
| Diarrhea | | | X | X | | | | | |
| Glossitis and stomatitis | | | X | X | | X | | | |
| Gums, sore | | | | X | | X | | | |
| Indigestion | X | | | X | | | | | |
| Nausea and vomiting and ptyalism | | | | X | | | | | |
| Teeth dyscrasias | | | | | | X | | | |
| Nervous and Mental | | | | | | | | | |
| Arsenical peripheral neuritis | | | | | X | | | X | |
| Amyotrophic lateral sclerosis and muscular atrophy | | | | | X | | | X | |
| Epilepsy | | | | | X | | | | |
| Hyperesthesia and paresthesia | | X | | X | | | | | |
| Muscular rigidity | | | | | X | | | | |
| Muscular dystrophy | | | | | | | | X | |
| Myasthenia gravis | | | | | X | | | | |
| Neuritis: alcohol, pellagra, cirrhosis, pregnancy | | X | | | X | | | | |
| Numbness | | X | | X | | | | | |
| Parkinsonism | | | | | X | | | | |
| Trigeminal neuralgia | | X | | | | | | | |
| Vertigo | | X | | X | | | | | |
| Walking: difficulty and awkwardness | | X | | | X | | | | |
| Depression, forgetfulness, confusion, delirium | | | | X | | | | | |
| Insomnia | | X | | X | X | | | X | |
| Irritability, nervousness and "neurasthenia" | | X | | X | X | | | | |
| Malaise | | | X | X | | | | | |
| Psychomotor drive | | | | X | | | | | |
| Weakness | | X | X | X | X | | | | |
| Malnutrition | | X | | X | | | | X | |
| Migraine | | | | X | | | | | |
| Blood | | | | | | | | | |
| Anemia with pellagra and pernicious anemia | | | | | X | | | | |
| Anemia with scurvy | | | | | | X | | | |
| Leukopenia and shift to left | X | | | | | | | | |
| Miscellaneous | | | | | | | | | |
| Cardiac failure | | X | | | | | | | |
| Edema | | X | | | | | | | |
| Conjunctivitis | X | | X | | | | | | |
| Keratitis | | | X | | | | | | |
| Night blindness | X | | X | | | | | | |
| Photophobia | X | | X | | | | | | |
| Xerophthalmia | X | | | | | | | | |
| Deafness | X | | | | | | | | |
| Scurvy | | | | | | | | | |
| Pellagra | | | | | | | | | |
| Beriberi | | | | | | | | | |

part low or low middle income groups. As a rule they came for the diagnosis of medical complaints; thus there was frequently a definite chronic disease in addition to poor diet, so that a high incidence of deficiency disease might be expected. The subjects lived not only in the San Francisco Bay region but often in other parts of the state. This study, made during the fall and winter of 1940-1941, includes consecutive entries. The only persons omitted were moribund patients or those with a language difficulty which rendered accurate history taking impossible. All patients received the general thorough "workup" which is carried out in a teaching university clinic, in addition to the special nutritional dietary history. Many subjects remember poorly or become fatigued during a long inquisition and answer carelessly; some seem to say what they think the doctor wants them to say, and finally there is the great difficulty of accurate estimates of amounts. The problem is further complicated by the duration of time during which the diet has been deficient: acute versus chronic deficiency. Be this as it may, the results of the present survey are given in table 1.

Points to be emphasized are, first, that the diet seemed inadequate in 22.9 per cent, or nearly one fourth of the whole group (although in some cases the deficiency was slight or pertained only to one category of

TABLE 4.—*Cases of Definite Vitamin Deficiency*

| Case | Age and Sex | Occupation | Disease Diagnosed | Dietary Deficiency | Signs of Vitamin Deficiency | Comment |
|---|---|---|---|---|---|---|
| 1 | 78 ♀ | None | Cancer of stomach proved by gastroscopy | Severe; little food, little dairy products, meat and greens; no fruit | Cheilosis, dry skin, sore tongue, weakness, numbness, paresthesia and difficulty in walking | Impression: neuritis associated with vitamin B deficiency |
| 2 | 75 ♂ | None | Cancer of stomach | Quantity of food low, especially in greens; otherwise seems adequate; vitamin supplements for 2 yr. | Weakness, dry itching skin, severe glossitis and moderate neuritis of peripheral type | Clearcut vitamin deficiency, multiple, especially thiamine and nicotinic acid |
| 3 | 64 ♀ | None | Tic douloureux; angina pectoris | Adequate except for little milk | Severe cheilosis with dry skin | Definite riboflavin deficiency; cleared up on riboflavin administration |
| 4 | 42 ♂ | Cook (unemployed) | Hypoproteinemia with edema; paratyphoid infection; possible hepatitis; achlorhydria | Not certain, but probably generally deficient | Edema; serum protein 5.4 Gm. per 100 cc. | Edema and low protein content of blood may have been related to vitamin deficiency; got well on high protein, high vitamin diet |
| 5 | 74 ♂ | Clerk | Coronary disease; cancer of thyroid with metastases | Deficient in total amount and especially in dairy products | Red, smooth tongue, fissuring at angles of mouth, weakness and emaciation | Definite mild vitamin B deficiency (especially riboflavin and nicotinic acid?); not improved by large doses of vitamins; desperately ill from cancer |
| 6 | 32 ♂ | Laborer | Functional indigestion | Diet seems fairly adequate except no whole grains and low in meat | Moderate cheilosis and some roughening of skin over nose | Mild riboflavin deficiency; improved promptly after taking riboflavin |
| 7 | 56 ♂ | Laborer | Cancer of lung; pleural effusion | Except for meat, diet is low in all components | Slight glossitis; dry skin and weakness | Symptoms probably partly due to cancer but probably a mild B deficiency |
| 8 | 50 ♂ | Cook | Desperately ill with pyloric stenosis from cancer | Vomiting; for 4 months has retained no food | Emaciation, edema, mild shark skin nose and moderate glossitis; serum proteins 3.8 Gm. per 100 cc.; some signs appeared after dextrose given intravenously | Edema and low protein content of blood possibly due in part to vitamin deficiency; mild vitamin B deficiency |
| 9 | 66 ♀ | None | Gastritis; malnutrition; edema; anemia | Low in calories; possibly poor absorption and anacidity for 10 yr. with diarrhea | Edema, anemia, weakness and dry skin; serum protein 4.7 Gm. per 100 cc. | Vitamin deficiency doubtless plays a part; no specific diagnosis |
| 10 | 65 ♀ | Housework | Vitamin deficiency; rheumatoid arthritis | Diet scant in vitamin B foods; occasional orange, bit of fish or egg; half pint milk daily | Severe anorexia; glossitis and sore gums, malnutrition, weakness and insomnia | Definite mild vitamin B deficiency |
| 11 | 52 ♂ | Musician | Chronic amebic colitis; diarrhea for several years | Low in calories, cereals and greens | Edema, low protein content of blood and malnutrition, glossitis | Certainly deficient in vitamin B as well as in proteins |
| 12 | 19 ♂ | Student | Acute ulcerative colitis | Diet good, but 9 weeks of severe diarrhea | Weakness, numbness and paresthesia of feet | Mild vitamin B deficiency associated with diarrhea |

history, which was taken in every case according to the outline presented as table 2.

Evidences of vitamin deficiency were checked on a special sheet (table 3) on which a survey of various symptoms and lesions and the specific vitamin alleged to be implicated was detailed. It was realized that some parts of the list were probably inaccurate; it was based on statements in the literature as of August 1940.

No chemical tests of vitamin saturation or excretion were made. It was felt that these cannot yet be fully interpreted in relation to clinical vitamin deficiency disease.

## RESULTS

1. *The Incidence of Defective Diets in the Present Group.*—One thing that one soon learns in work of this sort is the difficulty of obtaining a really satisfactory foods), and second, that the incidence of poor diet was much higher in the lower income group than in those with a better social service rating (46.0 per cent as against 20.7 per cent).

2. *Incidence of Clinical Evidence of Vitamin Deficiency.*—No case of full blown scurvy, beriberi, pellagra or keratomalacia was encountered. There were 4 instances of edema probably caused in part at least by poor diet. There were 12 cases, or 3.1 per cent of the whole group, in which definite but minor signs of clinical deficiency were noted. These cases are summarized in table 4. It is of note that some component of the vitamin B complex usually seemed to be lacking, and perhaps this is to be expected, as the early and minor stages of vitamin A and vitamin C deficiency show little in the way of evident clinical signs. There

were in addition 17 cases in which possible mild signs of vitamin deficiency were made out (table 5). Adding these to the definite cases, one gets a total of definite or suspected deficiency disease in 29, or 7.5 per cent of the whole group.

3. *Relation of Deficiency Disease to Defective Diet.*—The data are summarized in table 1 and show what one might expect: only an occasional patient with apparently normal diet gave evidence of vitamin deficiency, while about 20 per cent of those with inadequate diet had definite or suggestive clinical signs.

factory in southern California had clearcut evidence of one or more sorts of vitamin deficiency. It is on this account that many more accurate surveys should be made in various parts of the country. Be this as it may, it is quite clear that in the group herewith reported on the occurrence of clinical signs of vitamin deficiency was extremely low, even though many of the subjects were ill with diseases which might promote poor nutrition. It is of interest that there was an extremely good correlation of positive signs of deficiency with history of inadequate diet, which shows that even with a serious

TABLE 5.—*Cases of Doubtful Deficiency Disease*

| Case | Age and Sex | Occupation | Disease Diagnosed | Dietary Deficiency | Possible Signs of Vitamin Deficiency | Comment |
|---|---|---|---|---|---|---|
| 1 | 31 ♂ | Painter | Duodenal ulcer | No definite deficiency except that at times is on milk diet | Questionable magenta tongue; riboflavin deficiency? | Very doubtful if any clinical deficiency has been demonstrated |
| 2 | 52 ♂ | None | Cirrhosis of liver, advanced | Diet seems adequate * | Bruising, sore gums and weakness | Very doubtful if these symptoms are specific of vitamin deficiency |
| 3 | 56 ♂ | None | Gastric ulcer for years, verified at operation | Total intake low, especially in fruits, greens and meats | Undernutrition and dry skin; slight reddening of buccal mucosa noted by one examiner | No specific evidence of vitamin deficiency |
| 4 | 76 ♀ | None | Bronchial asthma, very severe; death | Diet adequate (history obtained from husband) | Ankle jerks not obtained; vibratory sense diminished over ankles; position sense absent in toes; tenderness of right calf | Possibly a very mild neuritis (vitamin $B_1$ deficiency?) |
| 5 | 56 ♀ | None | Tuberculosis of lung, pleura and pericardium, active | Total calories low; citrus fruits, whole wheat and meat low | Dryness of skin, slight reddening of buccal mucosa, malaise, weakness, insomnia and irritability | Possible mild vitamin B deficiency but symptoms probably from tuberculosis |
| 6 | 63 ♀ | None | Hypertension and anorexia nervosa | Diet generally low in calories; no milk; only small amounts of fruit and vegetables; no meat; for a while took yeast | Malnutrition, weakness, irritability, insomnia and mild gastrointestinal disturbance | In spite of poor diet has no specific signs of vitamin deficiency |
| 7 | 31 ♂ | Bartender | Duodenal ulcer | Adequate in meat and dairy products; low in fruits, greens and cereals | Smooth tongue, indigestion, occasional nausea and vomiting | Questionable mild vitamin B deficiency |
| 8 | 42 ♀ | None | Diarrhea and anacidity | Total calories low; otherwise diet seems adequate, but diarrhea may have caused absorption | Dry skin, weakness, malnutrition, irritability and slight macrocytic anemia | Questionable signs of specific vitamin deficiency |
| 9 | 69 ♂ | None | Hypernephroma with metastasis | Diet seems adequate | Slight smoothness of tongue | Questionable mild vitamin B deficiency |
| 10 | 56 ♂ | None | Arteriosclerotic heart disease; pyloric stenosis; neoplasms? | Low in total calories; otherwise diet seems adequate | Undernutrition, weakness, irritability and insomnia | Not definite for any specific deficiency |
| 11 | 62 ♂ | Caretaker | Dementia paralytica | Low in dairy products and cereals | Slight glossitis | Possible mild vitamin B deficiency |
| 12 | 64 ♀ | None | Rheumatic heart disease | Low total intake, especially greens and meat | Underweight, weakness, nervousness and anorexia | Very doubtful mild vitamin B deficiency |
| 13 | 34 ♂ | Plumber | Hodgkin's disease | Low in total amount; otherwise diet seems normal | Glossitis, weakness and malnutrition | Symptoms probably mainly due to Hodgkin's disease but tongue improved on vitamin B therapy |
| 14 | 57 ♂ | Molder | Gastric ulcer | Low in milk, fruits, greens and cereals | Dry skin and some redness of tongue | Very questionable mild vitamin B deficiency |
| 15 | 55 ♂ | Farmer | Gastric ulcer | Diet seems adequate; low total calories | Slight cheilitis and dry skin | Questionable vitamin B or A deficiency |
| 16 | 75 ♀ | None | Old age | Not remarkable; perhaps low intake | Slight redness and smoothness of tongue | Very doubtful slight vitamin B deficiency |
| 17 | 65 ♂ | Miner | Coccidioidomycosis | Low in calories and in all high vitamin foods | Weakness, edema, indigestion and dry skin | Possible mild vitamin deficiency; cannot define it definitely |

* This patient probably had deficiency of vitamin K.

## COMMENT

Recent surveys of vitamin deficiency disease have on the whole shown a disturbingly high incidence.[1] Most of these reports have been made by careful well trained investigators, and the results seem dependable. However, it is important to take into account the locality in which the survey is made, the particular population group and the criteria for diagnosis. Some of the statements made in the lay press, on the other hand, must be interpreted with caution, such as those claiming that 50 per cent of the employees in a certain disease, such as cancer, hepatitis and arteriosclerosis, deficiency disease does not readily supervene provided the diet remains adequate.

One of the most important practical aspects of nutritional disease is the question of variation in resistance to vitamin deficiency. It is well known that people do not all develop clinical signs with equal readiness; in many cases extremely poor diets may be tolerated for long periods before clinical evidences of disease occur.[2] This is well illustrated in the present study. As pointed

1. Jolliffe, Norman; McLester, J. S., and Sherman, H. C.: The Prevalence of Malnutrition, J. A. M. A. **118**: 944 (March 21) 1942.

2. Brenner, S., and Roberts, L. J.: Effect of Vitamin A Depletion on Young Adults, Federation Proc. **1**: 188 (March 16) 1942. Williams, R. D., and Mason, H. L.: Observations on Induced Riboflavin Deficiency in Man, ibid. **1**: 192 (March 16) 1942.

out in table 1, among 88 persons with defective diet only 11.4 per cent showed clinical signs of deficiency.

It is necessary to emphasize again some of the problems involved in surveys of this sort. First, the eliciting of a satisfactory accurate dietary history is at times difficult, if not almost impossible, and, second, the judgment as to whether minor but yet specific signs of vitamin deficiency exist must often be uncertain. How much stress can be placed on vague symptoms of weakness, fatigue, insomnia, poor appetite and so on? What is the significance of a little dryness or roughness of the skin or a slight eczematoid condition at the nasolabial fold? Even the therapeutic test is often difficult to interpret in persons with such dubious phenomena. Finally, if some of these minimal signs are the results of vitamin lack, how serious are the implications? These and many other questions still require careful evaluation.

SUMMARY

1. A survey was made of approximately 400 consecutive patients admitted to the clinic wards of Stanford University Hospital with reference to inadequate diet and signs of vitamin deficiency.

2. Approximately one fourth of these patients had been taking an inadequate diet.

3. Of those with inadequate diets, 11.4 per cent showed definite signs of vitamin deficiency.

4. Among 297 patients with adequate diets, only 2 instances of clinical vitamin deficiency were detected.

5. In the entire group the incidence of definite vitamin deficiency disease was 3.1 per cent.

## CARDIAC RESUSCITATION

### WITH REPORT OF A CASE OF SUCCESSFUL RESUSCITATION FOLLOWING AURICULAR AND VENTRICULAR FIBRILLATION

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Up to the present time, cardiac resuscitation has usually been attempted on patients who die in the operating room. With the increased knowledge of the physiology of the cardiorespiratory system and improvement in equipment, the possibility of cardiac resuscitation outside the operating room and particularly in warfare should become a reality. Being prepared for such occasions by having a definite plan of treatment and suitable equipment will result in a greater number of successful cases.

It is our purpose in this paper to review some of the methods of cardiac resuscitation, to present experimental and clinical evidence of the value of certain resuscitation procedures, to present a plan of treatment for cardiac or, better called, cardiorespiratory resuscitation and to report a case of successful resuscitation following auricular and ventricular fibrillation.

The physiology of the cardiovascular system and that of the respiratory system are so intimately connected and interdependent that changes in the functioning of one system are almost immediately registered by changes in the other, and, regardless of which was the site of the original dysfunction, cessation of the function of one will quickly lead to cessation of the other. In attempting resuscitation it should be remembered that it is necessary to revive the cardiovascular as well the respiratory system, since one cannot survive without the other.

The brain and the heart are the most sensitive of all the vital organs to anoxia, and permanent changes occur in the central nervous system from anoxia long before they do in other organs.

*Efficiency of Different Resuscitative Procedures*

| | Success | Failure | Success, per Cent |
|---|---|---|---|
| **Oxygen** | | | |
| 1. Manual artificial respiration | 6 | 5 | 55 |
| 2. Rhythmic inflation | 7 | 2 | 78 |
| 3. Rhythmic suction | 4 | 1 | 80 |
| 4. Resuscitation (rhythmic inflation and suction) | 21 | 1 | 95 |
| **Nitrogen** | | | |
| 1. Manual artificial respiration | 1 | 6 | 15 |
| 2. Rhythmic inflation | 2 | 10 | 17 |
| 3. Rhythmic suction | 1 | 4 | 20 |
| 4. Resuscitation (rhythmic inflation and suction) | 30 | 5 | 85 |

During severe anoxia permanent injury to the brain may occur within five to eight minutes, and if resuscitation is to be complete and permanent oxygenation of the brain cells is vital. Therefore adequate pulmonary ventilation is the first prerequisite in cardiac resuscitation and should be established immediately. Proper pulmonary ventilation may prolong the period of possible resuscitation beyond the five to eight minute limit and give more time for the restoration of the cardiac activity.

There are many ways of establishing pulmonary ventilation, the most important of which are manual artificial respiration, mouth to mouth insufflation and various mechanical resuscitators, some of which operate on a positive pressure and release principle and others utilize a positive pressure inflation together with a negative pressure deflation. Using the "asphyxial resuscitation"[1] test we have shown that the mechanical resuscitators which employ safe alternating positive and negative pressures (suck and blow) are the most efficient and successful, and this method is far superior to any other method of pulmonary resuscitation, as shown in the accompanying table. It is probably unnecessary to mention the importance of an unobstructed airway with any method of resuscitation.

The beating of the heart after death on mechanical stimulus has been known since the time of Vesalius, and the rationale of all cardiac resuscitation procedures is based on the fact that cessation of cardiac activity does not mean that the heart muscle is dead. By the very nature of its specific tissue the heart can be made to contract long after the death of the patient.

Kountz,[2] in a series of 127 remarkable perfusion experiments after death, was able to revive 65 human hearts, and of these 65, 48 (73.8 per cent) developed regular cardiac mechanism and beat for a period of two hours.

Acute cardiac cessation is conveniently classified into two groups: (1) arrest of stimulus formation, or the

From the Thoracic Surgical Service of the New York Medical College, Flower and Fifth Avenue Hospitals, and the Department of Thoracic Surgery of the Metropolitan Hospital.

1. Thompson, S. A., and Birnbaum, G. L.: The Phenomenon of Asphyxial Resuscitation, Proc. Soc. Exper. Biol. & Med. **41**: 203-204, 1941. Birnbaum, G. L., and Thompson, S. A.: The Mechanism of Asphyxial Resuscitation, to be published.

2. Kountz, William B.: Revival of Human Heart, Ann. Int. Med. **10**: 330 (Sept.) 1936.

so-called pacemaker failure, the result of which is cardiac standstill, and (2) electrodynamic dissolution of the cardiac cycle, of which ventricular fibrillation is an example.

Any attempt at cardiac resuscitation is always justified, and many such attempts have been successful even after considerable periods of inactivity have elapsed. Adams recently reported a twenty minute cardiac arrest with complete recovery.[3] It is our belief that a surprisingly large percentage of successful results will follow early and properly applied methods of cardiac resuscitation.

Among the many methods that have been reported as being successful in reviving the heart are sudden pressure on the heart made by sharp blows over the precordium, intravascular injections, intracardiac injections, mechanical stimulation by the insertion of a needle into the heart, electrical stimulation applied directly to the heart, mechanical inflation and deflation (suck and blow) of the lungs (experimental) and cardiac massage. The value of some of these procedures is quite clear, since, from the use of many different drugs. It is probable that the success in some instances was due in part, if not entirely, to the mechanical stimulation of the needle prick. Epinephrine is probably the most efficacious of the drugs used. In circumstances in which intracardiac injections might be employed, the absence of a drug should not deter the operator from attempting to stimulate the heart mechanically by inserting the bare needle into the myocardium. This mechanical injury to the muscle fibers sets up a reaction called an "action current of injury," [5] which in turn causes a contraction or extrasystole, and restoration of the normal pacemaker function may be the result.

The site of the injection is very important and should be in the right auricle for the following reason: [6] As the anoxia of the heart muscle increases the irritability increases, and any stimulus sufficient to develop an action current of injury may lead to flutter and then fibrillation. If the site of the injection is in the ventricle, then ventricular fibrillation may occur, which is incompatible with life. If the injection is in the auricle

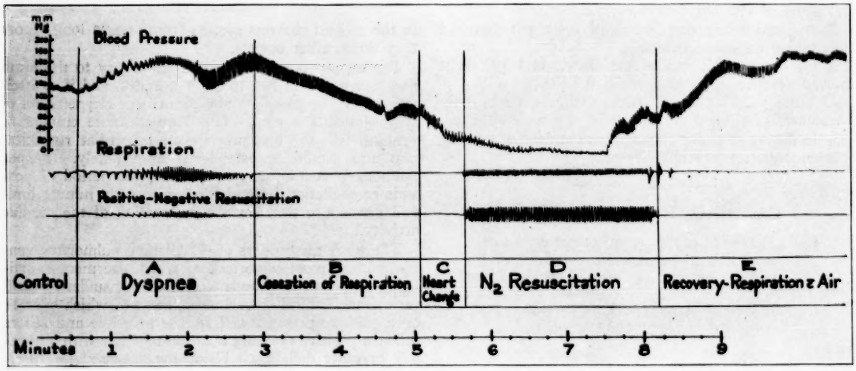


Fig. 1.—The phenomena of asphyxial resuscitation. Nitrogen inhalation asphyxia is produced by way of a leak proof intratracheal tube. After cessation of respiration and in the period of cardiovascular changes with a rapidly falling blood pressure, the lungs are rhythmically inflated and deflated with the same nitrogen which had just produced the asphyxia by means of a mechanical resuscitator of the suck and blow type. *A*, inhalation of 100 per cent nitrogen; this is the period of dyspnea. *B*, at the beginning of this period respirations have ceased; the blood pressure begins to fall. *C*, the heart beat is slower and somewhat irregular, and the blood pressure is falling rapidly. *D*, nitrogen resuscitation is started, as previously described, two and three-quarter minutes after respiratory cessation. The blood pressure continues to fall and approaches zero. Approximately one and three-quarter minutes after nitrogen resuscitation was started there was resuscitation of the cardiovascular system, as shown by the sudden and continued rise of the blood pressure. Spontaneous respirations occurred later, and use of the resuscitator was discontinued. The intratracheal tube at the end of *D* is exposed to the atmospheric air for the first time since nitrogen inhalation was started, approximately eight and one-half minutes. *E*, recovery.

and the value of the others is less obvious. The danger of any of these measures is of little account when the patient is, to all intents and purposes, already dead.

Cordelli [4] was able to induce cardiac contractions by repeated sharp blows over the precordium. This method is undependable and should be used only for a few seconds and while waiting for instruments and equipment before proceeding with some other method.

Intravascular injections are of no value when there is no movement of the blood stream. In conjunction with cardiac massage, however, it is likely that these drugs are moved on toward the heart and brain and may have some beneficial effect.

The first intracardiac injection in the human being was done early in the nineteenth century, and many cases of successful resuscitation have been reported and auricular fibrillation occurs, this is not incompatible with life and will respond to therapy.

Approach to the right auricle is through the third or fourth intercostal space on the right side, close to the sternum, and the needle is inserted in a downward and inward direction. The needle should be about 4½ inches long and reasonably stout. The possibility of injury to a coronary vessel during the intracardiac injection is small but definite, and if successful resuscitation occurs the patient should be observed for some time afterward for this possible occurrence.

Hyman [7] has shown the value of electrical stimulus applied directly to the right auricle and has developed

3. Adams, H. D., and Hand, L. V.: Twenty Minute Cardiac Arrest with Complete Recovery, J. A. M. A. **118:** 133 (Jan. 10) 1942.

4. Cordelli: Minerva med. **8:** 343, 1928.

5. Hyman, Albert, S.: Resuscitation of the Stopped Heart by Intracardial Therapy: Further Use of the Pacemaker, U. S. Nav. M. Bull. **33:** 205 (April) 1935.

6. Hyman, Albert S.: Intra-Auricular Puncture, J. A. M. A. **97:** 408 (Aug. 8) 1931.

7. Hyman, Albert S.: Resuscitation of the Stopped Heart by Intracardial Therapy: Use of the Artificial Pacemaker, Arch. Int. Med. **50:** 283 (Aug.) 1932.

an "artificial pacemaker" for use in cardiac standstill due to paralysis of the sinus node or arrest of stimulus formation.

Mechanical inflation and deflation of the asphyxiated dog's lungs has a massage effect on the heart and acts as a cardiovascular resuscitator. This is not due to the stimulating effect of oxygen, since cardiac resuscitation can occur from the inflation and deflation of the lungs with an asphyxiating gas (fig. 1). This active inflation and deflation of the lungs (using air or oxygen) is also the best manner of establishing and maintaining pulmonary ventilation.

In our animal experiments we have repeatedly found that manual massage of the heart is the most successful single procedure in reestablishing the normal heart contractions (figs. 2 and 3), and whenever this is possible in human beings it should be done. As a resuscitation method, cardiac massage was employed even before intracardiac injections. The earliest experience was in 1874, and one of the outstanding successes was reported by Lane in 1903.[8]

The approach to the heart for massage may be any of the following: (1) thoracic, (*a*) transpleural or (*b*) extrapleural, or (2) abdominal, (*a*) subdiaphragmatic or (*b*) transdiaphragmatic. The approach will be determined somewhat by the operation or circumstances present at the time of the cardiac cessation. If a thoracic operation is in progress the thoracic approach should be used, and if an abdominal operation is in progress the abdominal approach should be used. When no operation is being done the abdominal approach is desirable for several reasons: the thoracic approach takes longer; with the thoracic approach a closed system of pulmonary ventilation is necessary to overcome the effect of the open pneumothorax, and with the abdominal approach it is possible to establish manual artificial respiration if no other method is available. In case of ventricular fibrillation, direct exposure of the heart by the thoracic approach is preferable.

There is a definite place for prophylaxis of cardiac cessation. This is done by the preoperative injection of drugs that decrease the sensitiveness of the heart to vagal stimulation, particularly atropine, and by the attempt to eliminate or decrease the vagal reflexes through the local injection or topical application of procaine hydrochloride at the sites where these reflexes originate, particularly during operative procedures around the arch of the aorta, at the hilus of the lung, on the heart itself and during the insertion and removal of an endotracheal tube [9] (fig. 4).

Actual cardiac resuscitation must be done quickly and with a definite plan in mind, since valuable time may be lost when no plan is followed.

First and most important is the establishment and maintenance of proper pulmonary ventilation. This is best accomplished by a mechanical resuscitator using safe positive and negative pressures. Many operating rooms, however, are not equipped with such resuscitators, and the next best method is inflation and release of the lungs by making pressure on the anesthesia bag. This pressure should not be violent or excessive, as it is unnecessary and may damage the alveoli.

When cardiac cessation follows civilian injuries or in warfare, there is usually no resuscitation apparatus of any kind available, so manual artificial respiration should be started at once.

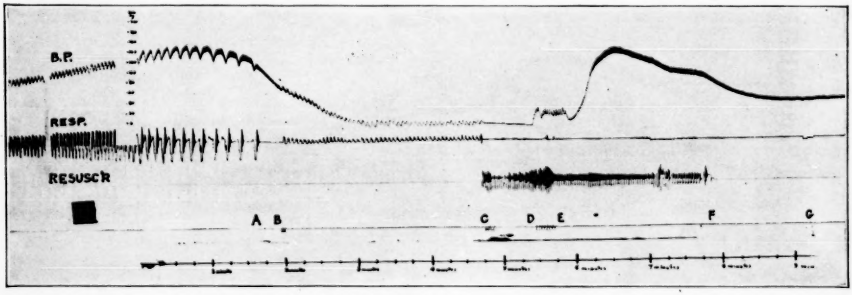


Fig. 2.—Resuscitation by the use of the resuscitator together with direct massage of the heart through the open chest. Mechanical obstruction asphyxia. *A*, respiration ceases. *B* to *C*, manual artificial respiration with oxygen inhalation unsuccessful. *C*, resuscitator with oxygen started; chest opened in the midline and direct heart massage started at *D* and continued to *E*, where regular heart beats resume. *F*, resuscitation discontinued. *G*, spontaneous respiration.

In thoracic operations with the chest open, cardiac massage can be easily and quickly done by grasping the heart and gently squeezing the ventricle, thus producing an artificial systole. If there is no response of the heart after one minute, the pericardium is opened and the massage is continued, producing about sixty artificial systoles to the minute. In this way with proper pulmonary ventilation the blood can be oxygenated and moved on to the heart muscle and the brain cells, and the extreme need for haste is now ove After another minute of massage and no cardiac contraction, 1 cc. of epinephrine (1:1,000) is injected into the chamber of the right auricle. If no epinephrine is available at the moment, the wall of the right auricle should be stuck with the bare needle. This mechanical stimulation may be sufficient to start the heart contracting. If an electrical apparatus of the "pacemaker" type described by Hyman is available, it should be used as soon as possible. This is also applied to the right auricle for best results. If the cause of the heart standstill can be determined and is still active (ligature

8. King, E. S. J.: Surgery of the Heart, Baltimore, William Wood & Co., 1941.

9. Reid, L. C., and Brace, D. E.: Irritation of the Respiratory Tract and Its Reflex Effect on the Heart, Surg., Gynec. & Obst. **70**: 157-162 (Feb.) 1940.

around the bronchus) it should be relieved, otherwise resuscitation may fail.

These measures are all used in conjunction with cardiac massage, and if the heart muscle is felt to "firm up" and begin to contract the massage is immediately discontinued. When no contraction has occurred after six to eight minutes, the routine just described is repeated. Artificial systole plus pulmonary oxygenation will sustain life for a long time, and the massage should not be abandoned as a failure until a forty-five to sixty minute period has elapsed.

When cardiac standstill occurs during an abdominal operation the first step is to insure pulmonary ventilation by the measures previously described or by manual artificial respiration if necessary. A few sharp thumps with the closed fist are administered over the precordium as soon as possible, as this mechanical stimulation may start the heart beating. In the meantime the operator should slip one hand under the diaphragm just beneath the heart. The abdominal incision is enlarged if necessary, and cardiac massage is begun by pushing up on the heart against the anterior chest wall. If no heart

When cardiac standstill occurs following injuries in civilian life or in warfare the possibility of successful resuscitation is remote, as there is usually no available apparatus for pulmonary ventilation or for cardiac resuscitation. However, a definite routine should be followed. If a resuscitator is available it is applied immediately; otherwise manual artificial respiration is begun. A few sharp thumps with the closed fist are administered over the precordium. If epinephrine is available, 1 cc. (1:1,000) should be injected into the right auricle, as previously described. If no epinephrine is available but a needle is, the needle should be inserted into the right auricle. The use of an artificial pacemaker at this time may be life saving. If no response is obtained in two or three minutes, a paramedian incision is made high up on the left side, beginning at the angle of Larrey, and this is carried through into the peritoneal cavity. The operator's hand is slipped under the diaphragm, and cardiac massage is started by pushing up on the heart against the anterior chest wall.

The latter procedure cannot always be done under aseptic conditions; however, one must remember that

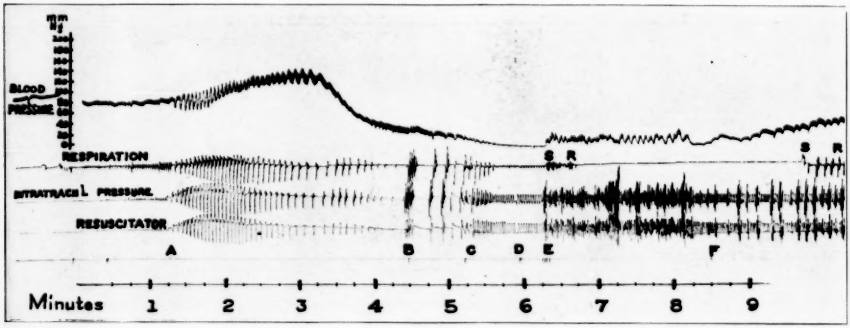


Fig. 3.—Resuscitation by external heart massage. *A*, nitrogen inhalation asphyxia through a leak proof intratracheal tube was started. *B* to *C*, asphyxial gasps. *C* to *D*, resuscitator with nitrogen was used. *D*, nitrogen discontinued and resuscitator continued with oxygen. *E* to *F*, external heart massage. *F*, heart beats have resumed. *G*, spontaneous respiration.

contractions occur after one minute of massage, the diaphragm and the adjacent pericardium are incised wide enough to admit one hand, and cardiac massage is continued. The same routine which was described for cardiac cessation in thoracic operations is now applied.

In going through the diaphragm it is important to avoid opening the pleura, unless provision has been made for a positive pressure pulmonary ventilation. Nicholson [10] recommends the following procedure in the abdominal approach for cardiac massage, since he says only the tip of the heart is compressed:

> An opening is made with a knife or a pair of scissors just behind the xiphoid process, between the attachments of the two sides of the diaphragm. There is a soft avascular spot here, and no damage is likely. . . . The thumb of the right hand is thrust through this opening and is now in the pericardium anterior to the heart. The heart is then compressed between the thumb, which acts by fixing the heart and preventing it slipping, and the fingers outside the diaphragm. . . . It is quite unnecessary to suture the hole in the pericardium.

10. Nicholson, John C.: Cardiac Massage, Brit. M. J. **2**: 385 (March 21) 1942

there is only one degree of death, and that is complete. The manner of its occurrence is immaterial, and any procedure that may obviate its occurrence is always permissible. Therefore time rather than asepsis is the essence of success.

The theoretically perfect setup for the treatment of cardiac cessation in warfare or civilian defense would be a "field resuscitator" with safe alternating positive and negative pressures which could be worked by a hand or foot pump, using ordinary air. This resuscitator should be light (weighing from 8 to 10 pounds) and small enough to be part of the standard equipment of each first aid station and to be carried along by stretcher bearers. Attached to this resuscitator should be a small artificial pacemaker of the type described by Hyman. This pacemaker need be no larger than a pocket flashlight and should contain batteries and a sterile needle electrode. With such a setup the first aid administrators would be able to attempt cardiac as well as respiratory resuscitation.

In many instances it may be clinically impossible to determine whether the cardiac cessation occurred as a result of standstill or ventricular fibrillation. In those

instances in which the differential diagnosis is impossible the routine which has been described should be followed, since fibrillation accounts for a smaller number of deaths.

When it is definitely known that ventricular fibrillation exists, an entirely different routine is necessary. Here again it is imperative to establish pulmonary ventilation immediately, as the following routine requires direct exposure of the heart and the use of an electrical defibrillator. Exposure of the heart if not already accomplished requires a certain amount of time, and not every operating room is equipped with a defibrillator; therefore the percentage of successful resuscitations in ventricular fibrillation will be small.

In 1899 Prevost and Batelli [11] demonstrated the ability to produce a cessation of ventricular fibrillation in the experimental animal's heart by the direct application of an electric current to the ventricle. More recently Beck [12] has devised and used a defibrillator. With this apparatus he shocks the heart, producing a definite cessation of the fibrillation and ventricular contraction or standstill. The heart is then shocked or massaged to produce the normal automatic contractions.

In ventricular fibrillation the most efficient method of resuscitation, according to Beck,[12] consists in the use of intracardiac injection of procaine hydrochloride followed by an electric shock. The method recommended by Beck is as follows:

> Five cc. of 2 per cent procaine is injected into the cavity of the right auricle or right ventricle. Massage of the heart moves the drug through the lungs, left side of the heart, aorta, coronary arteries and myocardial bed. . . . Two large electrodes of metal are placed one on each side of the heart and a shock of one to one and one-half amperes is sent into the myocardium. The current is ordinary electric light current with sufficient resistance in the current to reduce the amperage. The current is made and then broken after a fraction of a second. . . . Not infrequently the fibers go back into the state of fibrillation and the shock must be repeated. [If no contraction occurs] 1 cc. of epinephrine is used. . . . The heart is again shocked. [If no contraction occurs] 1 per cent calcium chloride in doses of 5 cc. [is] injected into the cavity of the right ventricle.
>
> The heart can be defibrillated. These methods are effective. It may require several attempts but if conditions are proper, such as the amount of oxygen, the tonus of the heart muscle and the irritability, the coordinated beat can be restored.

Scherf [13] has shown in animal experiments that ventricular fibrillation can be terminated by the intracardiac injection of a 1 per cent solution of potassium chloride. He [14] recommends the use of a 1 per cent solution of potassium chloride in human beings by intracardiac injection plus cardiac massage. The initial dose is 5 cc., followed in one minute by another injection of 5 cc., followed in one minute by a third injection of 5 cc. if no response has been obtained.

Ordinarily the injection of epinephrine plus massage of the heart will not stop ventricular fibrillation. However, in case 2, reported herewith, massage plus the possible benefit of neosynephrin plus pulmonary ventilation were successful.

In the final analysis the success of cardiac resuscitation will depend on (1) the cause of the cardiac cessation, (2) the condition of the heart before cessation occurred and (3) the elapsed time before proper resuscitation measures are attempted. When the cause of the cessation is due to vagal reflexes arising outside the heart the possibility of resuscitation is good with a healthy heart muscle. When myocardial disease existed prior to cessation the possibility of resuscitation is decreased. When the cessation is due to ventricular fibrillation the possibility of resuscitation under ordinary conditions is remote, and this possibility is further decreased by the fact that fibrillation does not usually occur in a previously healthy myocardium. Fortunately the greater number of cardiac failures seen during operations, in warfare, in subasphyxiating gas attacks and in electrical shock are due to standstill rather than fibrillation [15] and it is in this group that the largest number of cases of successful resuscitation will occur.

In cardiac cessation the odds in favor of resuscitation decrease with each minute that passes before proper measures are applied. The stakes are high—a human life.

The half hearted attempts at resuscitation should be replaced by early and bold attempts at resuscitation in which a definite routine is used. The feeling that once the heart has stopped the patient is gone and nothing will help should be replaced by the knowledge that a human life can and may be saved, and any attempt is justifiable.

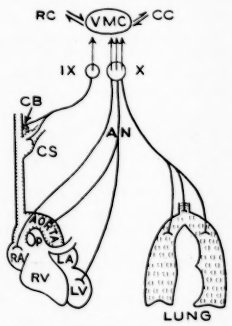


Fig. 4.—Afferent nerves concerned in the regulation of circulation and respiration. These nerves are from the trachea, bronchi and lungs, from the arch of the aorta and the carotid body and sinus. The sinus nerve joins the glossopharyngeal. The aortic and pulmonary nerves join the vagus. Stimuli arising at the periphery of these nerves may reflexly cause cardiac standstill or respiratory cessation. *RC*, respiratory center. *VMC*, vasomotor center. *CC*, cardiac center. *IX*, glossopharyngeal nerve. *X*, vagus nerve. *CB*, carotid body. *CS*, carotid sinus. *AN*, aortic nerve. (Modified from Wright.)

REPORT OF CASES

CASE 1.—W. P., a man aged 59, was admitted to the Flower and Fifth Avenue Hospitals on Sept. 10, 1941 with a diagnosis of carcinoma of the right lung. The diagnosis was substantiated by biopsy of material obtained by bronchoscopy, and he was subjected to a right pneumonectomy on September 16. A preoperative electrocardiogram revealed no abnormal findings.

With the patient under endotracheal ether and oxygen anesthesia, a posterior lateral approach was made. The pulmonary artery and veins had been doubly ligated and cut between ligatures. While the peribronchial tissues were being dissected at approximately one and one-half hours after the start of the operation, the heart became irregular and ceased to contract. The anesthetist was immediately notified and oxygen (100 per cent) was substituted for the anesthetic. Positive pressure and release pulmonary ventilation was carried out by the anesthetist about twenty times a minute. At the same time manual massage of the heart was started by the operator, who placed his left hand over the right lateral and posterior surface of the mediastinum and compressed the heart up against the posterior

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13. Scherf, David, and Boyd, Linn J.: Clinical Electrocardiography, St. Louis, C. V. Mosby Company, 1940.
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15. Turner, K. B.: Mechanism of the Human Heart, Am. Heart J. **6**: 743 (Aug.) 1931.

surface of the sternum. In one minute the heart was felt to contract, and the massage was discontinued. The heart contractions became stronger and the rhythm was regular. The operation was continued five minutes after the cardiac standstill had occurred. The peribronchial tissues were now infiltrated with 2 per cent procaine hydrochloride close to the carina. The bronchus was ligated and severed ten minutes after the operation was resumed. Immediately on cutting across the bronchus the heart again ceased to beat. Again the anesthetist was notified and 100 per cent oxygen was substituted for the anesthetic, and pulmonary ventilation was instituted by manual compression and release of the anesthetic bag. At the same time manual massage of the heart was again started. After one minute when no heart contraction had occurred, 1 cc. of epinephrine (1:1,000) was injected into the right auricular chamber and manual massage of the heart was continued. One minute after the epinephrine was injected the heart was felt to contract, and the massage was discontinued. The beat became stronger and the rhythm regular, and the operation was continued to its successful conclusion, approximately one and one-quarter hours later. Twenty minutes after the operation was finished the endotracheal tube was removed and the patient was moved from the operating table to a stretcher. He immediately became cyanotic, and respirations and pulse stopped simultaneously. A bronchoscope inserted after a few minutes allowed a small thick plug of mucus to be aspirated from the remaining bronchus. All additional resuscitative measures failed.

The first cardiac standstill was quite apparently due to a vagal reflex from the plexus surrounding the bronchus. Although procaine hydrochloride infiltration allowed a further dissection of the peribronchial tissues without any cardiac disturbance, yet the reflex again became active causing cardiac standstill when the bronchus was severed. The speculation as to the possibility that atropine given intravenously after the first cardiac standstill may have prevented the second cardiac standstill is worthy of mention.

This case illustrates the quick response of the heart to early massage. The death of the patient may have been due to the fact that the original cause of the cardiac standstill was still active or it may have been due to anoxia from the mucous plug in the bronchus.

CASE 2.—*Successful resuscitation following auricular and ventricular fibrillation.*

W. B., a Negro aged 57, was readmitted to the Metropolitan Hospital on Sept. 11, 1941 for a carcinoma of the middle third of the esophagus. On July 24 a gastrostomy had been performed under cyclopropane anesthesia without any complication. On August 18 an esophagectomy was performed. Before the operation the heart action was regular and the electrocardiogram showed no abnormality.

Intratracheal cyclopropane anesthesia was used and begun at 2 p. m. At 2:15 p. m. cardiac fibrillation was noted and the anesthetist administered 1 cat unit of digifolin by hypodermic injection. At 2:25 the operation was begun. A posterior lateral approach was made through the seventh left intercostal space. At 2:35 the heart was inspected and found to be definitely fibrillating (auricular) and making irregular and tumultuous contractions. The administration of cyclopropane was discontinued and ether-oxygen was used as the anesthetic. Because of the seriousness of the lesion it was decided to continue the operation. An attempt was made to free the esophagus. All during the operative procedure the heart continued to beat in a most irregular fashion. The beats became weaker, and at 3:45 there was suddenly no longer any expulsive beat of the ventricle although it continued to twitch and fibrillate. The movements of the ventricle were irregular, incoordinated and independent of one another; there was no single wave of movement. Control of respirations had been taken over by the anesthetist at 3:30, or fifteen minutes before the heart stopped beating, and now oxygen (100 per cent) was substituted. Manual heart massage was immediately started, and ventricular fibrillations could be felt by the operator's hand as well as seen by the operator and several assistants and observers. After three minutes of heart massage with no contraction, 2 cc. of neosynephrin and 1 cc. of nikethamide were injected intravenously. Within one minute the heart was felt to contract, and massage was discontinued. The contractions became stronger, although the beat was still totally irregular and the auricles continued to fibrillate. The operation was then continued. Because the growth of the esophagus had infiltrated the lung and the descending aorta, operation was finally discontinued and the chest closed in the usual manner. The heart continued to fibrillate and the pulse was irregular until 9 p. m., or five hours after the operation was finished; then the pulse became regular.

The immediate postoperative reaction and recovery were satisfactory in every respect after the pulse became regular. The patient died on the eighteenth postoperative day from pneumonia. The postmortem examination showed a "bronchopneumonia of the left lung and carcinoma of the esophagus with infiltration of the left lung and thoracic aorta." The microscopic diagnosis was "epidermoid carcinoma."

The fibrillation was evidently brought on by the cyclopropane anesthesia, as it was first noticed five minutes after the administration of cyclopropane had been started. A preoperative electrocardiogram showed no abnormal findings, although on two occasions there was a clinical impression that fibrillation was present. The fibrillation was confined at first to the auricle and suddenly spread to the ventricle followed by cessation of any expulsive contraction, although the fibrillating fibers could be seen and felt. Manual cardiac massage had been continued three minutes before the intravenous injection of neosynephrin and nikethamide (no defibrillater was available). Within one minute after the injection, the ventricular fibrillations gave way to actual contractions. It is decidedly questionable whether sufficient time had elapsed for the drugs to be moved on to the heart by artificial systole. It is possible that the resuscitation may have been due entirely to the cardiac massage and pulmonary ventilation. On resuscitation, auricular fibrillation immediately returned and continued for five hours after the operation before the pulse became regular.

It has been assumed from animal experimentation that manual cardiac massage would not resuscitate a fibrillating ventricle. This is the first reported case we have been able to find of successful resuscitation with operative recovery of the patient following cardiac cessation due to auricular and ventricular fibrillation.

CASE 3.—H. M., a white girl aged 13 years, was admitted to the Metropolitan Hospital on June 12, 1941 with a history of pulmonary abscess and empyema four years previously, at which time a rib resection had been performed. After examination a diagnosis was made of cystic bronchiectasis of the upper and lower lobes of the left lung, atelectasis of the lower lobe and bronchocutaneous fistula. A pneumonectomy was performed on July 31.

Endotracheal cyclopropane anesthesia was administered. One hour and fifteen minutes after the operation was started, the dissection of the hilus was begun and atropine $\frac{1}{150}$ grain (0.4 mg.) was injected at this time. This was followed by 1 per cent procaine hydrochloride injected into the hilar tissues. Because of some irregularity of the heart the anesthetic was changed to ether. For the next thirty minutes the respirations were unsatisfactory and there was some cyanosis of the lips and finger tips. To improve pulmonary ventilation, control of the respirations was instituted by the anesthetist. During the dissection of the hilar tissues there was noticed a twitching

of the right arm and right leg and particularly on manipulation of the mediastinum. These twitchings lasted for twenty-five minutes. The heart action became weaker, and despite the controlled respirations the patient was moderately cyanotic. Two hours and forty minutes after the operation was started and while the mediastinal dissection was still being done the heart ceased to beat. Manual massage of the heart was immediately started, and one minute later 1 cc. of epinephrine (1:1,000) was injected into the right auricle. Massage was continued, and one minute later the ventricle was felt to contract and massage was discontinued. The contractions became stronger, and the heart resumed its normal function. Mediastinal dissection was continued, and thirty minutes later, when the bronchus was ligated before being severed, ventricular standstill occurred again. Cardiac massage was immediately started, and after two minutes 1 cc. of epinephrine was injected into the right ventricle. Massage was continued and after three minutes the ventricle was felt to contract and massage was discontinued five minutes after it was started. The heart again resumed its normal activity, and the operation was completed forty-five minutes later (total operative time approximately four hours). This patient never regained spontaneous respirations, and it was necessary to continue artificial pulmonary ventilation. Approximately one and one-half hours after the operation was finished the heart stopped beating and the patient died.

This patient had evidenced some difficulty in pulmonary ventilation continuously after the hilus dissection had begun and was continuously cyanotic. The cause of the twitching of the right arm and leg may have been from cerebral anoxia or from an embolism, either air or blood clot. The failure of the respiratory center was probably due to anoxia. The cardiac cessation on both occasions was quite evidently a vagal reflex, and this was active in spite of the atropine by hypodermic and the local injection of the procaine hydrochloride. On both occasions, however, the heart responded to massage and epinephrine.

CASE 4.—J. B., a Negro aged 56, was admitted to the Metropolitan Hospital on Sept. 18, 1940 with a Janeway gastrostomy which had been performed on June 26 for carcinoma of the middle third of the esophagus. On September 30 an esophagectomy was performed. A left transpleural approach was made. A preoperative electrocardiogram had revealed some myocardial damage.

Intratracheal cyclopropane was the anesthetic. Two hours after the operation was started, while the esophagus was being freed from under the arch of the aorta, ventricular standstill occurred. Cardiac massage was immediately started, and pulmonary ventilation with 100 per cent oxygen was maintained by the anesthetist. After two minutes 1.5 cc. of neosynephrin was given intravenously and cardiac massage was continued. Three minutes later the heart was felt to contract and massage was discontinued. The contractions were weak, and no blood pressure could be recorded for at least one hour following. The operation was continued, the esophagus was removed with the growth and the operation was successfully concluded one and one-half hours after the ventricular standstill had occurred.

The immediate postoperative condition was fair, but on the third day after the operation the patient became seriously ill and died of pulmonary edema.

Three minutes elapsed after the neosynephrin was administered intravenously before ventricular contraction occurred; this was sufficient time for it to be moved on to the myocardium, and it was probably of some benefit.

This case again illustrates the benefit of early and continued cardiac massage plus pulmonary ventilation. The cardiac standstill was due to reflexes from the vagus started by dissection around the arch of the aorta.

# THE MENACE OF "SILENT" OVARIAN CARCINOMA

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By "silent" I mean without symptoms—without any indication to the patient that a serious process is present. Patient after patient is seen with an extensive growth of long duration but with only a short period of local symptoms. The first visit to the physician shows a large growth or ascitic fluid from peritoneal carcinosis. The advancing carcinoma causes only such minor disturbances that the patient hardly notices them. Thinking back, when questioned, she recalls that the abdomen has been a little larger for a year or so or that there was bloating or some frequency of urination, but only in the last few weeks was there enough disturbance to make her feel that perhaps an examination was advisable. Some examples from my experience will serve to illustrate the point.

## REPORT OF CASES

Mrs. S., aged 56, had a gradual loss of weight for two years but no local symptoms till a few months before consulting a physician, and even then there was only indefinite discomfort in the abdomen and back. Abdominal examination showed a mass in the left side projecting up from the pelvis, and the patient was sent for operation. The operation revealed an extensive carcinoma of the ovary, which had already invaded irremovable structures. The main tumor was removed and roentgen therapy was given for the extensions. Repeated roentgen treatments prolonged life in fair comfort for a year.

Mrs. M., aged 70, had noticed gradual enlargement of the abdomen for a year and a half, with some loss of weight, but there were no localizing symptoms except indefinite discomfort in the lower part of the left side of the abdomen. The first examination revealed a large cystic mass filling the pelvis and extending to the umbilicus. Operation showed an ovarian cyst which was carcinomatous and with deep extensions. The primary growth was removed, and roentgen therapy was given for the irremovable portions.

Mrs. H., aged 52, had come under my care at the age of 47 for treatment of a retrodisplaced myomatous uterus with some prolapse and menstrual irregularity and hot flushes. At that time she was put on conservative treatment and directed to return in two months. She did not return for five years because, as she stated, "There was no special disturbance, and I felt well right along until some months ago." The principal symptom when the patient came at the age of 52 was enlargement of the abdomen. She thought this had come on gradually, but in the last two weeks it had become well defined and was accompanied with discomfort and an occasional pain. Examination showed pronounced ascites with some masses in the pelvis. Operation revealed general abdominal carcinosis of ovarian origin. No structure could be removed except a specimen for microscopic diagnosis.

Mrs. P., aged 47, had noticed enlargement of the abdomen for two months, with a feeling of pressure, soreness and frequency of urination for six weeks. Examination showed a pelvic mass extending half way to the umbilicus. At operation I found a carcinoma of the right ovary with extension to the uterus and other ovary and tube and also to the adherent appendix and abdominal wall. The main mass was removed along with the uterus, the other ovary and tube, the appendix and a specimen from the involved abdominal wall. In each of the structures mentioned, including the abdominal wall specimen, the extension of carcinoma was confirmed by microscopic examination. Postoperative roentgen therapy was employed,

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with unexpectedly good results. The operation was in 1933, and the patient is still well and strong and without evidence of recurrence. The patient was a physician's wife. Her sister had died of ovarian carcinoma and her mother of cancer of the stomach. In spite of these facts favoring close observation, the growth of the ovarian cancer was so "silent" that it had extended into surrounding structures before there was any intimation of its presence.

Miss R., aged 48, was a patient for whom, at the age of 43, I had performed a hysterectomy for myoma with right salpingo-oophorectomy and appendectomy, and recovery was without special incident. Five years later she was sent by her physician for treatment of a pelvic tumor extending almost to the umbilicus. She had noticed some pressure in the abdomen for about a year but gave little thought to it. An increase in the pressure discomfort finally caused her to go to her physician, who found the tumor. Operation showed extensive abdominal carcinosis originating in the left ovary. No structure could be removed. Repeated roentgen treatments kept the patient in fair comfort for nearly a year.

The lesson of this case is that I should not have left an ovary at age 43. I thought then that it was advisable, but I know better now.

Mrs. G., aged 55, went to her physician because she had noticed discomfort in the left side of the lower part of the abdomen off and on for a month or two. Examination showed a tumor the size of a fist filling the left side and central portion of the pelvis. Operation revealed a carcinoma of the left ovary. It had already spread to adjacent organs and into irremovable structures. The main mass was removed, and with roentgen therapy the patient lived for a year and eight months.

Mrs. S., aged 55, had noticed some constipation and nausea and frequent urination for several months and a slight bloody discharge for two weeks. She was three years past the menopause. Examination revealed a pelvic tumor extending up to within 1½ inches of the umbilicus. Operation showed extensive abdominal carcinosis, originating in the right ovary and involving adjacent structures so deeply that nothing could be removed except the laboratory specimen. Repeated courses of roentgen treatment produced temporary benefit over a period of two years.

Mrs. M., aged 70, stated that for about a month she had noticed intermittent pain and soreness in the abdomen, particularly when lying on either side. There had been constipation for the past year and considerable bloating, but less lately. She had lost 7 pounds (3.2 Kg.) in the last two months and also noticed some frequency of urination. Examination showed an irregular mass in the left side and central portion of the pelvis and extending up to the umbilicus. The diagnosis was carcinoma of the left ovary with general abdominal carcinosis. Gastrointestinal x-ray examination showed intestinal involvement. As the surrounding penetration was clearly too extensive for curative operation and there were no obstructive symptoms or severe pain necessitating palliative operation, the patient was given roentgen therapy to check the growth as much as possible. Repeated roentgen treatments kept her fairly comfortable for six months.

Miss L., age unknown, was seen about a year after the menopause. She was a rather peculiar individual, and never did reveal her age. She had been having vague intermittent abdominal discomfort for six months, with a feeling of pressure and some frequency of urination, and it was an increase of these minor discomforts in the last two months which caused her to seek medical advice. Examination showed a pelvic mass extending half way to the umbilicus. The patient was very stout, and deep palpation was unsatisfactory. There was general tenderness in the lower part of the abdomen, where irregular nodules could be felt. Operation revealed general abdominal carcinosis of ovarian origin. Nothing could be removed except the specimen for microscopic diagnosis. Roentgen therapy was advised as a palliative measure, but the patient preferred not to take it. She continued in fair comfort for a considerable time and died ten months after discovery of the growth.

Mrs. C., aged 46, had noticed gradual enlargement of the abdomen for several months, with bloating, occasional pains, constipation and some frequency of urination but no well defined symptoms. Examination showed the abdomen enlarged by ascitic fluid and a deep pelvic mass adherent in the posterior cul-de-sac. Gastrointestinal x-ray examination eliminated intestinal growth, and gallbladder visualization indicated normal functioning. Operation revealed general abdominal carcinosis originating in an ovary. The involvement was widespread and deep, and no structures could be removed except a specimen for microscopic examination.

Miss B., aged 49, was still menstruating fairly regularly. She stated that she was "perfectly well" up to three weeks preceding her visit, at which time she noticed that the abdomen was enlarged, making the clothing somewhat tight. In these last two or three weeks there were also pains in the abdomen and considerable backache, and she decided to consult a physician. Examination revealed the abdomen distended with ascitic fluid and a large mass extending up from the pelvis. Operation showed the pelvis filled with an ovarian carcinoma, which had extended deeply into the surrounding structures and upward in the abdomen even into the liver. Only a specimen for microscopic examination could be removed. The patient preferred not to take roentgen therapy. She lived nine months after discovery of the growth.

Mrs. P., aged 64, had noticed enlargement of the abdomen over a considerable period without particular discomfort, but for the three weeks preceding her visit there had been an increasing feeling of fulness and pressure, which caused her to consult a physician. The examination revealed a pelvic mass extending to 2 inches above the umbilicus. Operation showed a large ovarian cyst with some solid portions and also a smaller growth in the other ovary. Deep in the pelvis about the cyst there were dense adhesions of doubtful character. I finally succeeded in removing both ovarian tumors along with the tubes and the corpus uteri. Microscopic examination showed the ovarian tumor of each side to be malignant, and postoperative roentgen therapy was given. The operation was in September 1940, and so far the patient is well and without evidence of recurrence, but the outlook is not good.

## COMMENT

These 12 cases show the symptomless progress to extensive involvement which represents the natural history of ovarian carcinoma. Some patients are fortunate enough to have a coincident disease which takes them to a physician, who in the course of routine pelvic examination discovers the silent growth before it has progressed beyond removal. Most of the favorable cases of ovarian carcinoma are discovered in this way. Occasionally some early complication of the growth causes pain which leads to the examination. With these fortunate persons I am not dealing here. My purpose in this paper is to focus attention on the symptomless onset and symptomless progress of uncomplicated ovarian cancer. It is ordinarily a slow growing tumor, which penetrates into irremovable structures before the appearance of warning symptoms. The cases cited represent the experience of just one physician for a short period of thirteen years, 1929 to 1942. Multiply this by the number of gynecologists of extensive practice and add the numerous operations for late ovarian cancer by other gynecologists and by general surgeons and add also the number of patients who die of "ascites" and "abdominal cancer" without recognition of the ovarian growth, and you get some idea of the magnitude and importance of this "silent" menace.

WHAT SHALL WE DO ABOUT IT?

At present we are confronted with a form of creeping death which defies early discovery and progresses to incurability despite all efforts: carcinoma of the involuting ovary. Much excellent work has been done by gynecologists in investigating the etiology, pathology, diagnosis and treatment of ovarian cancer. But still most patients consult a physician when the growth is past cure and with a history of only recent symptoms. How can this situation be attacked effectively?

Physicians had to deal with a somewhat similar problem of fatal delay in carcinoma of the cervix uteri, and in that connection there were two steps which opened the path to the objective and which are now contributing greatly to the saving of lives. One of these steps is the removal of tissue presenting a condition that makes it specially susceptible to cancer development, that is, the removal of chronic cervicitis or other chronic cervix irritation by conization or conical excision before cancer starts; the other step is periodic examination to detect early evidence of cancer or of chronic irritation that may lead to cancer. Of course many improvements have been made also in the treatment of discovered cancer of the cervix, but the major part of the great advance in preventing deaths from that disease must be credited to these two steps. Much remains to be done in making these two procedures a part of the working rules of every physician, but that process is proceeding apace and each year adds to the widening circle of those who incorporate these life saving measures into their daily practice.

I feel that in seeking to reduce deaths from carcinoma of the ovary one must rely largely on these same two steps, namely removal of tissue which has become specially susceptible to cancer development and periodic examination to detect lesions of which the patient is not aware. To comprehend the situation one must squarely face three grim facts: First, a large proportion of patients with ovarian carcinoma consult physicians too late for cure; second, in some cases the patient in whom one leaves an involuting ovary at abdominal operation dies later of ovarian cancer, and, third, many women who are now active and comfortable and apparently well are carrying cancer of an ovary. A favorable feature is that even with considerable enlargement which could be easily detected on deep vaginoabdominal palpation, the growth may still be limited to removable structures. But women with this condition will wait for examination till they notice symptoms and then die of the disease in spite of all that science can do.

As I see it, the greatest contribution the physician can make toward the lessening of these fatalities is the practical application in his daily work of two rules: (1) removal of the involuting ovaries whenever the abdomen is opened at an age and under circumstances which permit such removal; (2) insistence on regular periodic pelvic examination of patients who ask us to assume responsibility in regard to their health.

1. When does ovarian involution begin? The menopause (complete cessation of menstruation) occurs usually between the ages of 44 and 47, with exceptions somewhat below and above these limits. The climacteric (gradual involution of the ovaries) begins two or three years before the menopause and extends some years after it. Though there is considerable individual variation as to age of onset of ovarian involution, a reasonable rule would be to apply this safety measure in all abdominal operations when the patient has reached the neighborhood of the age of 42. Some physicians would perhaps put this average age later and some would put it earlier. Also special conditions are found, and special desires of the patient are of course to be taken into consideration. What I wish to emphasize is not this or that particular age but the fact that in an abdominal operation in a woman in or near the period of ovarian involution the matter of ovarian removal should be given most careful consideration. The involuting ovaries have fulfilled their reproductive and endocrine functions. They are no longer an important part of the economy but vestigial structures which carry a special tendency toward cancer—and toward a particularly dangerous form of cancer, in that it develops to an incurable stage without warning symptoms.

The realization of the necessity of adopting this safety measure has been obscured and delayed by the various arguments for retention of an ovary. In the first place, there is the excellent surgical rule to do no more operating than necessary—to remove no structure without a definite reason of sufficient importance to justify the additional operative risk and any probable upset in physiology. Again, the great importance of the ovaries during the span of their physiologic activity projects about them a halo which tends to obscure the fact that they are only temporary organs that cease to function after a certain period. Again, there is the desire to lessen the hot flushes and other disturbances of ovarian cessation by preserving ovarian tissue even though it is functioning only partially. Still again there is the natural desire of the patient that an ovary be saved if practicable. These are all valid arguments and have long influenced decisions, but through careful observation and bitter experiences I have come to realize that the danger of cancer development in the involuting ovary outweighs all these arguments for leaving an ovary in an abdominal operation in the age of involution.

Though necessary for reproduction and accessory activities connected with child bearing, the ovaries are not the basic factor in sex determination and sexual response which is so generally assumed. The sex of a person is determined long before the ovaries are formed; sexual response continues long after ovarian function has ceased, and, as I have clearly shown in case reports,[1] normal female desires and instincts and outlook on life and sexual response may exist without ovaries, with testicles instead of ovaries, and without either. As noted in reporting one of my cases, "It may be stated that in this case and in the several cases reported the absence of ovaries and the presence of testicles seemed to exert little or no influence on the strong female desires and responses. Despite the hindering presence of testes and later the lack of sex glands altogether, the patient's feminine personality continued the even tenor of its way."

2. At what period is periodic pelvic examination required in connection with cancer of the ovary? That is a question to which I have given considerable study, in the endeavor to minimize trouble and expense to the patient and yet maintain a fair security against undis-

1. Crossen, H. S.: A Problem in Sex Classification, Am. J. Obst. & Gynec. **38**: 123, 1939.

covered ovarian cancer. In considering periodic examinations in connection with the subject of cancer of the cervix we [2] stated the following in our textbook:

> It is important to work out a practicable plan. The local examination should be made often enough to reasonably exclude irritation that would favor cancer development, and yet no more often than is necessary for safety. The choice of interval should be such as to appear reasonable to most patients when the matter is explained to them. The choice of a rather long interval which appears to the patient so reasonable that she returns regularly will go much further toward preventing cancer than the choice of an interval so short that the patient neglects returning and finally gives up regular examination. Considering the various angles of the matter, it seems to us that a reexamination once a year from age 35 to 55 is a reasonable rule to incorporate in our advice to these patients in connection with uterine cancer.
>
> The probability of the patient's cooperation in the idea of a regular yearly examination may be enhanced by pointing out that this twenty year period is one of change in body structure and function, and also that many authorities are recommending a general examination yearly as a safety measure to determine how the various vital organs are standing the wear and tear of life's activities. This explanation reenforces and emphasizes the idea of regular general examinations, of which the local examination is a part.

The special period for ovarian cancer begins somewhat later, extending from the ages of 40 to 60. Also more frequent examinations are required. Cancer of the cervix is usually preceded by a period of chronic cervicitis, which can be seen on examination. This gives ordinarily a leeway of many months of appreciable lesion before actual cancer development. But with cancer of the ovary there is no such preceding warning. The cancerous infiltration and enlargement of the ovary is the first appreciable lesion and requires prompt operation to save the patient. Hence in the period from 40 to 60 years of age pelvic examination is advisable every six months instead of once yearly, as may suffice before and after that period.

Of course, a practicable rule of action must take into consideration the patient's natural reluctance to examination not definitely indicated by troublesome symptoms. Here is where the leadership of the physician comes in. By tactful instruction that causes no undue apprehension but rather a comfortable feeling of added safety the patient may be made to see the advisability of local examination as part of the general examination on which responsible advice to her must be based. There are few patients who do not appreciate the relief from anxiety afforded by a careful examination or who will not see the health advantage and eventual economy of regular examinations which would detect disease in a curable stage instead of waiting for symptoms which signal incurability. However, experience has shown that the most serious defect in the machinery of preventive medicine lies just at this point. Patients do not return for the necessary examinations. Why? Until this question is answered and the import of the answer is recognized and applied in a practical way, little headway will be made in preventing deaths from ovarian cancer or other obscure diseases. Hence it is advisable to warn the physician of this pitfall in the seemingly clear path.

2. Crossen, H. S., and Crossen, R. J.: Diseases of Women, ed. 9, St. Louis, C. V. Mosby Company, 1941, p. 557.

## CAUSE OF FAILURE

The splendid educational campaigns conducted by the American Society for the Control of Cancer and other interested agencies have gone far toward preparing the public for the advice which the individual physician could give to his patients in regard to regular examinations, including pelvic examinations. Such examinations at regular intervals are necessary for the discovery of uncomplicated ovarian carcinoma in a curable stage as well as of other hidden lesions. Do we explain to our patients the advisability of returning at certain intervals for this examination, putting the advice in a practical way so that they understand it and can profit thereby? The answer in general must be that we do not do so. The reasons for not doing so are many and varied, and, though each is insignificant compared to unrecognized cancer development, in the aggregate they have sufficed to prevent the physician from taking up this matter with each patient in the practical and effective way with which he takes up her other health problems.

The responsibility of the individual physician to his patients for persistent educational efforts in this direction is very great, and that responsibility must be recognized and met. Measuring up to this responsibility will require a severe wrench from the ordinary and established custom of treating only evident lesions and waiting for ovarian cancer to develop to the evident stage before giving consideration to the matter. Radical advances usually require radical departure from established custom and from easy following of the beaten path. The great medical triumphs over apparently insurmountable difficulties were not attained by the complacent and satisfied but by those who were ready to make courageous struggle against the apathy of easy popular custom and the deadening inertia which operates against radical advance.

The excellent general educational campaigns referred to have done a great deal to cause women to come for the first examination, but what has been done to educate the examined patient to return at proper intervals for the reexaminations which are so necessary? There is a tendency to blame the patient when she comes with a cancer that is past cure. But one cannot expect the patient to know the necessity of returning when she is without symptoms unless she is told to do so. She has not taken a course in medicine. She is depending on her physician to give her the medical information necessary to guard her health in this respect. The influences of the general educational agencies referred to are most helpful as far as they go, but the return of our patients for the regular pelvic examinations which we know are needed depends largely on what we say to them in the course of our medical advice.

In the last analysis, it rests with the physician to educate his patients to an appreciation of the fact that certain growths may develop in the pelvis without warning symptoms and hence that regular periodic examinations are necessary and urgent as a safety measure. The particular form of advice as to return will of course vary with different physicians and with different patients. With some patients the simple advice to return at a certain time will be followed, while others may wish to be told the reasons, urgency, and so on, before deciding the matter. The important thing is to take the time and thought required to put the advice to each patient who should return in such a way that she will benefit from it, and not simply as some general remark to act as a salve to conscience should she return years afterward with an incurable ovarian carcinoma.

Another item in this immediate connection should be mentioned. Patients with the best of intentions of returning as advised may fail through oversight at the time because of the press of other activities. An effective aid at this point is the prearranged notification, used so generally in business and already to some extent in medical and dental work. When the advice to return at a certain time is given, a card for the patient is placed under that month in the file, and at the appointed time a brief reminder note is sent. Patients are notified regularly on financial matters, and it is certainly in order and would be an important step in advance to notify them regularly on this medical matter which is a life saving measure.

In connection with these pelvic examinations there arise of course many questions of differential diagnosis and difficult decisions as to whether or not there is evidence of ovarian carcinoma or other lesion requiring operation. Those items do not come within the scope of this paper, but there is one associated point to which attention should be called. When one is doing a vaginal operation, such as curettage, conization, radium treatment or plastic work, it is very important to make careful examination of the ovarian regions, so that any associated lesion there may be discovered. Such examination under anesthesia or analgesia is of course particularly important in stout patients, in whom deep palpation otherwise may be so difficult that a small mass may escape detection. Also the recording in the operative note of the exact conditions in the pelvis at this deep examination will prove exceedingly helpful in determining the significance of conditions found later.

SUMMARY

Symptomless onset and symptomless progress to incurability constitute the natural history of ovarian carcinoma. Earlier discovery is due to some incidental associated condition or to a pelvic check-up examination.

The aggregate of deaths from this cause is large, much larger than is generally appreciated. To the known cases must be added the unrecognized ones with death certificate designations of "ascites" and "abdominal cancer." A large proportion of the cases of general abdominal carcinosis originate in an ovary.

The silent character of the onset and progress of ovarian cancer seals the doom of patients with this condition unless measures that are really effective against the serious difficulties of the situation are put into practice. The following three steps are advisable and urgent in reducing deaths from this insidious disease:

1. Removal of the involuting ovaries whenever the abdomen is opened under circumstances which permit of such removal.

2. Insistence on regular periodic pelvic examination of patients who ask the physician to assume responsibility in regard to their health. These periodic examinations for silent ovarian carcinoma should be made every six months, instead of once yearly, which was formerly supposed to provide adequate safety. One must give the time and thought necessary to make this advice of real benefit to each patient instead of simply throwing out some general remark to act as a salve to conscience should the patient return later with incurable cancer.

3. Utilization of every opportunity afforded by anesthesia for a minor vaginal operation to make deep accurate palpation of the ovarian areas, the findings to be recorded in the operative note for future reference and comparison.

University Club Building.

## SULFAGUANIDINE IN TREATMENT OF DYSENTERY (BACTERIUM FLEXNERI) CARRIERS

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Attempts with sulfaguanidine in the treatment of bacillary dysentery were destined to follow the more or less successful trials with the previously discovered sulfonamide compounds, namely, sulfanilamide,[1] sulfapyridine [2] and sulfathiazole,[3] and also the highly encouraging experimental studies of Marshall and his associates.[4] These workers noted that sulfaguanidine combined the advantages of free solubility in water together with poor absorption from the gastrointestinal tract. Further clinical investigation has confirmed the tendency of the usually administered dosages to saturate the intestinal content without exceeding a relatively low level of concentration in the blood.

In a well controlled clinical study, Lyon [5] described the remarkably rapid improvement which followed the administration of sulfaguanidine in 17 of 23 cases of acute bacillary dysentery of the Flexner type. The ability of the drug to destroy permanently the organism in the intestinal tract was not evaluated in this study, probably because the treated patients were inhabitants of a number of communities in the tristate area of West Virginia, Ohio and Kentucky, where the disease is endemic and reinfection is presumably common.

The report of Rantz and Kirby [6] on the use of sulfaguanidine in the treatment of dysentery carriers stresses particularly the necessity for evaluating any treatment of this infection as much for its ability to eliminate completely the organism from the stool as for its ability to relieve clinical symptoms. In 9 of 11 cases, dysentery bacilli (Bacterium flexneri) disappeared from the stools during treatment and did not return over periods varying from thirty to ninety days.

A particularly good opportunity for gaging the efficacy of sulfaguanidine from both these points of view and with the added advantage of comparison with a large, untreated group of controls from a previous outbreak presented itself at the Norwich State Hospital.

### FIRST OUTBREAK (1939-1940)

During an outbreak of acute bacillary dysentery (B. flexneri, variety strong), which occurred in the fall and winter of 1939-1940, the organism was isolated at least once from the stools of 38 patients. Eighteen of the patients were considered to have the disease, since they presented as well the symptoms of bloody diarrhea, elevated temperature and frequently nausea or vomiting. The remaining 20 were classified as carriers from the onset. The patients were all women, for the most part

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3. Ching, R. E.; Warr, O. S., Jr., and Witherington, J. B.: Sulfathiazole Treatment of Bacillary Dysentery: Nineteen Cases, J. Tennessee M. A. **34:** 171 (May) 1941.
4. Marshall, E. K., Jr.; Bratton, A. C.; White, H. J., and Litchfield, J. T., Jr.: Sulfanilylguanidine: A Chemotherapeutic Agent for Intestinal Infections, Bull. Johns Hopkins Hosp. **67:** 163 (Sept.) 1940.
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6. Rantz, L. A., and Kirby, W. M. M.: The Use of Sulfaguanidine in the Treatment of Dysentery Carriers, J. A. M. A. **118:** 1268 (April 11) 1942.

of very advanced age. The outbreak was of the contact type and confined to a single building, the women's infirmary.

Since this outbreak occurred before the era of chemotherapeutic management of bacillary dysentery, the only treatment which the patients received was supportive, with a particular effort made to combat dehydration. Both patients and carriers were quarantined. Release followed a succession of six negative cultures of the stool obtained at least twenty-four hours apart.

TABLE 1.—*Statistical Data on the First Outbreak (Patients Untreated)*

| Patient | Positive Stool Cultures: Age | Number | Days | Total Number of Stools Cultured |
|---|---|---|---|---|
| 1 † | 70 | 1 | 1 | 13 |
| 2 * | 82 | 1 | 1 | 10 |
| 3 † | 76 | 1 | 1 | 8 |
| 4 † | 55 | 3 | 3 | 15 |
| 5 * | 64 | 3 | 3 | 16 |
| 6 * | 33 | 3 | 3 | 31 |
| 7 † | 56 | 3 | 4 | 10 |
| 8 † | 85 | 2 | 5 | 25 |
| 9 * | 52 | 5 | 7 | 14 |
| 10 * | 62 | 9 | 10 | 29 |
| 11 † | 57 | 2 | 10 | 27 |
| 12 * | 69 | 5 | 12 | 16 |
| 13 † | 66 | 2 | 12 | 13 |
| 14 † | 66 | 3 | 17 | 20 |
| 15 † | 69 | 5 | 26 | 26 |
| 16 * | 64 | 3 | 27 | 17 |
| 17 * | 80 | 3 | 30 | 23 |
| 18 † | 59 | 5 | 30 | 18 |
| 19 * | 52 | 4 | 30 | 16 |
| 20 † | 82 | 2 | 30 | 17 |
| 21 * | 70 | 5 | 30 | 14 |
| 22 * | 85 | 5 | 33 | 20 |
| 23 † | 27 | 4 | 33 | 16 |
| 24 * | 73 | 3 | 33 | 22 |
| 25 † | 77 | 4 | 34 | 16 |
| 26 † | 70 | 8 | 45 | 32 |
| 27 † | 16 | 3 | 49 | 15 |
| 28 * | 44 | 7 | 60 | 23 |
| 29 * | 54 | 6 | 60 | 23 |
| 30 * | 78 | 3 | 60 | 21 |
| 31 † | 54 | 10 | 60 | 28 |
| 32 * | 23 | 9 | 90 | 26 |
| 33 † | 76 | 7 | 120 | 35 |
| 34 † | 71 | 7 | 155 | 30 |
| 35 * | 76 | 17 | 395 | 66 |
| 36 † | 68 | 16 | 515 | 63 |
| 37 † | 82 | 33 | 730 | 72 |
| 38 * | 50 | 67 | 790 | 89 |

* Patient with dysentery.
† Healthy carrier.

It may be seen from table 1 that the stools of 9 patients became negative for B. flexneri in less than ten days. In 7 patients from ten to thirty days were required for a final reversal of the stools to negative. Twenty-two of the group of 38 patients, representing over 57 per cent, retained the bacillus in the gastrointestinal tract for one month or longer.

### SECOND OUTBREAK (1941-1942)

After an interval of two years, a second outbreak of acute bacillary dysentery, again of the contact type, started in the same building and spread to neighboring dormitories, involving a few occupants of these buildings. None of the patients of the previous epidemic came down with the infection or acquired the organism anew.

Of the 33 patients treated with sulfaguanidine, 15 were classified as having the disease and 18 as symptomless carriers (table 2). All patients but 1 were elderly. From their stools Shigella paradysenteriae, variety strong, was recovered, the same organism involved in the previous episode. The only male inmate of the group (patient 27) showed the army variety of B. flexneri in his stool.

With few exceptions (patients 1, 2, 3, 4, 14 and 27) administration of the drug was started within four days following receipt of the first positive stool specimen by the laboratory. The same course of treatment was followed in every instance, whether or not the patient was classified as having the disease or as a carrier. Four Gm. daily of sulfaguanidine by mouth was administered in divided doses for one week. No ill effects were observed, and in no case was it necessary to stop use of the drug prematurely.

In all patients the stool collected at the end of the period of treatment was negative for B. flexneri. In 6 patients (1, 14, 17, 21, 23 and 30) the bacillus disappeared from the stool before the prescribed total of 28 Gm. of the drug had been given. Since it was frequently impossible to obtain stool specimens at will during the course of treatment, this group was no doubt actually more numerous.

In all but 4 instances (patients 3, 11, 14 and 22) from ten to thirty-eight consecutive stool cultures remained negative over an average period of one hundred and five days. The 4 exceptions were subjected to a second course of 28 Gm. of sulfaguanidine and responded promptly with a consecutive series of twelve to fourteen negative stools.

TABLE 2.—*Statistical Data on the Second Outbreak (Patients Treated)*

| Patient | Positive Stool Cultures Prior to Use of Sulfaguanidine: Age | Number | Days | Negative Stool Cultures Following Use of Sulfaguanidine: Number | Days | Recrudescence |
|---|---|---|---|---|---|---|
| 1 * | 71 | 3 | 19 | 14 | 117‡ | |
| 2 * | 67 | 3 | 11 | 13 | 112 | |
| 3 * | 78 | 3 | 11 | 8 | 54 | 14 consecutive negative |
| 4 * | 67 | 5 | 21 | 12 | 99 | stools over 50 days |
| 5 * | 65 | 4 | 4 | 12 | 109 | following second |
| 6 * | 76 | 2 | 4 | 15 | 116 | course of drug |
| 7 † | 60 | 2 | 4 | 13 | 119 | |
| 8 † | 45 | 1 | 2 | 14 | 121 | |
| 9 † | 59 | 2 | 3 | 13 | 121 | |
| 10 † | 64 | 1 | 2 | 15 | 115 | |
| 11 † | 59 | 1 | 2 | 3 | 16 | 12 consecutive negative |
| 12 † | 58 | 2 | 3 | 10 | 118 | stools over 98 days |
| 13 † | 61 | 1 | 3 | 14 | 119 | following second |
| | | | | | | course of treatment |
| 14 † | 68 | 3 | 7 | 3 | 15‡ | 14 consecutive negative |
| 15 * | 61 | 2 | 3 | 13 | 113 | stools over 82 days |
| 16 * | 80 | 1 | 2 | 14 | 116 | following second |
| 17 † | 67 | 1 | 3 | 14 | 116‡ | course of treatment |
| 18 † | 76 | 1 | 2 | 15 | 109 | |
| 19 † | 81 | 1 | 3 | 14 | 106 | |
| 20 † | 39 | 1 | 3 | 13 | 100 | |
| 21 † | 58 | 2 | 3 | 12 | 105‡ | |
| 22 * | 74 | 1 | 2 | 2 | 27 | 14 consecutive negative |
| 23 * | 73 | 2 | 2 | 15 | 111‡ | stools over 61 days |
| 24 * | 17 | 1 | 3 | 25 | 99§ | following second |
| 25 * | 52 | 1 | 2 | 14 | 97 | course of treatment |
| 26 * | 44 | 2 | 4 | 20 | 91§ | |
| 27 * | 38 | 5 | 13 | 10 | 73 | |
| 28 † | 26 | 1 | 3 | 22 | 91§ | |
| 29 † | 79 | 1 | 3 | 15 | 81 | |
| 30 * | 69 | 1 | 3 | 38 | 90‡§ | |
| 31 † | 37 | 2 | 4 | 14 | 74 | |
| 32 † | 43 | 2 | 3 | 25 | 75§ | |
| 33 † | 40 | 1 | 5 | 12 | 44 | |

* Patient with dysentery.
† Healthy carrier.
‡ Stools became negative for B. flexneri during treatment.
§ Stools intermittently positive for Eberthella typhosa.

During the routine of culturing for Shigella, the stools of 5 patients (24, 26, 28, 30 and 32) of the group intermittently revealed colonies on bismuth sulfite agar which agglutinated as Eberthella typhosa. This high incidence of typhoid carriers within a group of

dysentery convalescents may have been partially due to the fact that the carriers of the two organisms were isolated within the same building. The stools of 2 patients (24 and 28), who were also recognized as typhoid carriers prior to the administration of sulfaguanidine, continued positive for Eberthella. The drug failed to affect this organism, although the disappearance of the dysentery bacillus from the intestinal tract was prompt and apparently permanent. We have not yet attempted a deliberate trial with sulfaguanidine in an effort to reduce the number of typhoid carriers.

### COMMENT

The severity of dysentery due to the Flexner group of bacilli varies widely. The disease in the outbreaks described in the present study did not represent the acute fulminating type. It was relatively mild and, as pointed out by Hodge,[7] of the type which is important owing chiefly to its tendency to persist if untreated and to its infectivity.

The advantages of a measure which will reduce the period of the carrier state or eliminate it entirely are obvious in any community. In a large hospital for mental illness where patients, through their untidiness and lack of cooperation, may become particularly dangerous carriers, the period of isolation may be shortened for the patient, and the duration of the quarantine which is imposed on the entire dormitory or institution may be reduced considerably.

As seen in table 1, 57 per cent of the group of patients which did not receive sulfaguanidine continued to carry the bacillus in their stools a month or more after it was first detected. Of this number, 31 per cent were persistent carriers, i. e. those who harbored the bacilli for more than three months after the beginning of the disease. In sharp contrast to this, a single course of sulfaguanidine effected the complete disappearance of dysentery bacilli from the stools of 88 per cent of the patients involved in the second outbreak. This result was obtained uniformly during or at the end of treatment with moderate, nontoxic amounts of the drug and persisted for an average of one hundred and five days.

Since it is well known that the presence of B. flexneri in carriers has a tendency to be intermittent, the bacillus being excreted for one or two days in succession and then not again for weeks or more, the usual criteria of a few successive negative stools following the termination of the acute illness cannot be accepted as a guaranty against the reappearance of the organism.

Despite the administration of sulfaguanidine, 4 of 33 patients, or 12 per cent, underwent a recrudescence of their infectivity. Although this number is relatively small, it indicates that, even with the use of this drug, caution must be exercised in deciding when the carrier state is definitely over.

### SUMMARY AND CONCLUSIONS

Two outbreaks of bacillary dysentery caused by the same organism (B. flexneri, variety strong) and involving comparable groups of patients occurred in 1939-1940 and in 1941-1942 respectively at the Norwich State Hospital.

The 38 patients with positive stools of the first outbreak did not receive chemotherapy. Fifty-seven per cent of this group maintained their infectivity for a month or longer.

The stools of 88 per cent of the 33 patients involved in the second outbreak remained negative for the dysentery bacillus over an average period of one hundred and five days following administration of 28 Gm. of sulfaguanidine.

The reappearance of B. flexneri in the stools of 4 patients after a first course of treatment indicates the necessity for continued laboratory examinations for several weeks after an apparent reversal to negative.

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## STAPHYLOCOCCIC INFECTION SIMULATING SCARLET FEVER

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Scarlet fever was identified by both Sennert and Sydenham as a separate clinical entity during the seventeenth century, but discussions of its etiology remained purely speculative until two centuries later. In 1869 Hallier [1] isolated streptococci from the blood of several patients with scarlet fever, and in the eighties W. H. Power [2] and Klein [3] traced epidemics of the disease to milk obtained from cows with streptococcic mastitis. It is of considerable historical interest that the modern concept of the pathogenesis of scarlet fever was formulated as early as 1893. Thirty years before the classic experiments of the Dicks [4] and Dochez,[5] Bergé [6] had written:

> Scarlet fever is a local infection; the infectious agent which produces it is the streptococcus, in one of its virulent forms; in the common type of scarlet fever, which one might call pharyngeal, the streptococcus multiplies in the pharyngeal and tonsillar crypts and apparently secretes an "erythrogenic" toxin whose diffusion throughout the organism produces the eruption of the skin and mucous membranes . . . in puerperal and surgical scarlet fever, the local infection is either in the uterus or in the wound. . . . As for the immunity conferred by scarlet fever, it exists only for the cutaneous manifestations.

The evidence which Bergé was able to adduce for his theory did not prove to be convincing, and the toxin concept was not generally accepted until the contributions of numerous investigators [7] finally cul-

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minated in the convincing experiments of the Dicks and Dochez in 1923.

Scarlet fever was for several years considered to be due to a soluble toxin secreted by a specific strain of hemolytic streptococcus, often referred to as Streptococcus scarlatinae. Workers both in this country [8] and in England,[9] however, showed that toxin production was not a property limited to any single type or strain of hemolytic streptococcus; they advanced conclusive evidence that "the production of an erythrogenic toxin capable of eliciting an erythematous skin reaction in man . . . is a property of hemolytic streptococci of human origin in general." [10]

That the erythrogenic toxin of the hemolytic streptococcus represented a single antigenic unit was never questioned until the usage of the Dick test became widespread and reports of occasional anomalies and apparent inaccuracies in the test appeared in the literature.[11] It was then that Park and Spiegel [12] suggested, on the basis of careful titration experiments, that there might be more than one toxin associated with scarlet fever. Trask and Blake [13] in 1933 described cases of scarlet fever apparently due to toxins which were not neutralized by standard Dick antitoxin, and Hooker and Follensby [14] isolated from patients with scarlet fever two strains of hemolytic streptococcus producing toxins which were antigenically different. Reviewing the subject of streptococcus toxins in 1936, Hooker [15] predicted that still other toxins capable of producing scarlet fever would eventually be isolated and identified.

Although scarlet fever is now known to be caused by more than one toxin produced by many different types and strains of beta hemolytic streptococcus, little attention has been paid to the possibility that the disease may be due to toxins produced by organisms other than the hemolytic streptococcus. Our purpose in the present paper is to report a case together with immunologic experiments which suggest that scarlet fever may occasionally be caused by staphylococcus toxin. Attention is also drawn to the literature which has accumulated in support of this concept.

## REPORT OF CASE

M. W., a 15 year old white schoolgirl, American born, was admitted to the Osler Clinic of the Johns Hopkins Hospital on the evening of July 3, 1941 complaining of pain in the left thigh of four days' duration and of fever for three days.

The family history revealed no familial disease; no other member of the family had suffered from a recent infection or had had any known contact with contagious disease in the recent past.

The past history and system review revealed only a transient pyelitis at the age of 7 months, measles at 3 years and chickenpox at 4 years. A tonsillectomy had been performed when the patient was 12. Colds were of moderate frequency and were only occasionally accompanied by sore throat. Menarche occurred six months before admission, and menses were regular. Diphtheria, scarlet fever and acute rheumatic fever were specifically denied.

The patient had been in the best of health until two weeks before admission. At that time she contracted a mild infection of the upper respiratory tract, accompanied by a very slight sore throat; there was no fever; the patient continued to attend school, and with no therapy other than a rare gargle with saline solution she apparently recovered completely in ten days.

Four days before admission, while watering the garden, she noticed an aching pain in her left thigh. She knew of no trauma, recent or remote, to account for this pain. It was accentuated by flexion of the hip. The discomfort, at first mild, increased to the extent that she was unable to sleep and cried aloud.

The pain persisted on the following day, and she was unable to eat her meals. Her physician found her temperature to be elevated and prescribed rest, use of a local liniment and salicylates by mouth. This therapy resulted in some regression of her symptoms for several days; but on the day preceding admission the pain in her leg increased strikingly in intensity, and she had a severe shaking chill and experienced nausea and vomiting. When the passage of another twenty-four hours revealed no amelioration of her condition, hospitalization was advised. At no time in the course of this illness did the patient notice any sore throat, nor did there appear any evidence of a respiratory infection.

Physical examination on admission showed that the patient was well developed and well nourished and mildly disoriented. Obviously she was acutely ill. Her temperature was 105 F., pulse 120, respiratory rate 30 and blood pressure 90 systolic and 40 diastolic.

The most striking feature on inspection was a diffuse erythematous rash, which at first was most evident on the trunk and shoulders but which later advanced peripherally. The rash consisted of erythematous macules, which blanched readily on pressure and were most profuse in the folds of the axilla, groins and antecubital fossae. There was no rash on the face, but the latter was diffusely flushed and there was well defined circumoral pallor. On the soft palate and extending onto the hard palate there was an intensely red, fine enanthem. The tongue was dark red, and on its surface hypertrophic papillae stood out producing the classic "raspberry" appearance.

The pupils were round, regular and equal and reacted to light and in accommodation. The fundi were normal. There was some congestion of the conjunctivas. The nares were clear, and there was no evidence of infection in the pharynx. The neck was supple, and the lungs were clear. There was slight but definite, nontender enlargement of the superficial lymph nodes. The heart was not enlarged. The pulse was rapid and regular, and there was a blowing systolic murmur over the base of the heart. The second pulmonic sound was louder than the second aortic sound. Pulses were soft, bounding and equal. The abdominal examination was normal save for slight distention. Inspection of the genitalia showed no discharge or other abnormality. Reflexes were normal. No petechiae or furuncles were present.

There was diffuse tenderness over the lateral aspect of the left thigh and pain on flexion of the thigh. No local swelling could be discerned, and both legs were of equal size. There was no tenderness along the courses of the great veins, nor was there any venous engorgement.

The laboratory findings on admission were as follows: The red blood cell count was 4.99 million, the hemoglobin 12.5 Gm.

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10. Zinsser, Hans; Enders, J. F., and Fothergill, L. D.: Immunity. Principles and Application in Medicine and Public Health, ed. 5, New York, Macmillan Company, 1939, p. 581.

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per hundred cubic centimeters, and the hematocrit reading 41 per cent. The white blood cell count was 13,100 with 78 per cent polymorphonuclear leukocytes. The corrected sedimentation rate was 31 mm. in one hour. Examination of the urine revealed a specific gravity of 1.015, no sugar, a 2 plus reaction for albumin and strongly positive reactions for acetone and diacetic acid. The centrifuged urinary sediment contained 5 to 8 white blood cells per high power field and an occasional red blood cell and hyaline cast. The serologic reaction for syphilis was negative.

On the patient's admission, a diagnosis of scarlet fever was made by the intern, isolation precautions were instituted and the case was reported to the city board of health. All who saw the patient made the same diagnosis. Material from the throat and blood were taken for culture and parenteral fluids administered.

During the night the patient's temperature fell to 103.2 F. and on the following morning she was well oriented and said she did not have a sore throat but continued to complain of pain in the left thigh. The rash covered her entire body, save for the circumoral pallor and the diffusely flushed face. The throat culture taken the preceding evening showed no beta hemolytic streptococci, and preliminary inspection of the blood culture revealed many gram positive cocci. Surgical consultants found no localizing signs to account for the pain in her leg. In the absence of pharyngeal infection, in a well defined case of scarlet fever with bacteremia, it was concluded that the patient was suffering from nonpharyngeal scarlet fever and that chemotherapy was urgently indicated. Accordingly, sodium sulfadiazine was given intravenously and then orally, so that on the following morning a blood level of 13.8 mg. per hundred cubic centimeters was attained. The same evening the patient's temperature rose to 107.6 F. following a chill. After a test of serum sensitivity, 18,000 units of Lederle's scarlet fever antitoxin was administered intramuscularly. The temperature fell precipitously to 98 F. and a simultaneous fall in blood pressure was arrested by an infusion followed by a transfusion of citrated whole blood.

A final report on the first blood culture revealed the gram positive cocci to be hemolytic Staphylococcus aureus.

On the next morning the second blood culture showed 54 colonies of hemolytic Staph. aureus per cubic centimeter. The hemolytic streptococcus was never isolated from repeated cultures of the throat, vagina, urine or blood.

Within the twelve hours following the administration of the scarlatinal antiserum there was a striking fading of the rash, and the patient's tongue began to show desquamation. Her temperature, however, slowly rose again to 103 F. Although a presumptive diagnosis of acute osteomyelitis with septicemia was made, it was not until July 6, her fourth hospital day, that evidence of definite localization of the infection became manifest. Repeated search, both at this time and subsequently, failed to show either petechiae or furuncles, although her blood culture remained persistently positive for hemolytic Staph. aureus. The microscopic hematuria disappeared immediately after admission, as did the ketonuria.

On the morning of the fourth hospital day well localized pain and tenderness developed over the lateral aspect of the left greater trochanter. With the patient under gas, oxygen and ether anesthesia an incision was made over the trochanter and deepened to the bone itself, without any pus being encountered. When the cortex of the bone was drilled, pus under pressure welled out through the drill holes. Cultures of this pus showed a hemolytic Staph. aureus identical with that isolated from the blood stream. Adequate drainage was established, and the wound was packed open. Intensive chemotherapy was continued; a high blood level of sulfadiazine was maintained and parenteral fluids and another transfusion of citrated whole blood were given.

After operation the patient's course was one of continued improvement, although her temperature remained significantly elevated for almost a week, and her blood culture did not become permanently negative until the eighth postoperative day.[16] Her wound drainage, at first profuse, steadily diminished, and the wound was completely healed over by September 27. Because of the danger of the development of other foci, chemotherapy was continued for a total of three and one-half weeks; no other focus developed, and the only lesion shown by roentgen rays was a localized area of bone destruction in the upper end of the left femoral shaft.

On her fourteenth hospital day desquamation of the palms, soles, fingers and toes began and continued for more than a week. This desquamation was identical with that normally associated with scarlet fever.

Three and one-half weeks after admission, in spite of the fact that daily examinations of the urine had revealed no blood or albumin, the patient suddenly voided grossly bloody urine, which showed a 2 plus reaction for albumin. There was, however, no edema and no rise in blood pressure. Although it was thought that the hematuria was probably due to sulfadiazine, the possibility of a postscarlatinal acute glomerulonephritis was considered. The results of chemical examination of the blood, an electrocardiogram, venous pressure and a roentgenogram of the chest were normal, and the discontinuance of chemotherapy followed by the forcing of fluids resulted in the voiding of completely normal urine within four days. Shortly thereafter the hip was slowly mobilized and the patient was allowed to return home.

Antistreptolysin titer determined shortly before the patient's discharge was 500.[17]

## EXPERIMENTAL

When repeated and careful search in this case failed to reveal any evidence of the presence of the beta hemolytic streptococcus, the properties of the organism repeatedly isolated from the patient's blood stream, and also from her left femur at operation, were investigated. The infectious agent was identified as a typical strain of hemolytic Staphylococcus aureus and was found to be coagulase positive and to ferment mannite.

In order to determine whether this strain of staphylococcus produced an erythrogenic toxin, a sterile filtrate was prepared using the methods described for the preparation of Dick toxin.[18] After the filtrate had been transferred aseptically to sterile vials, its sterility was confirmed by culture, and the vials were placed in the icebox for several months. The erythrogenic power of the filtrate was estimated by injecting intracutaneously 0.1 cc. of various dilutions made with sterile isotonic solution of sodium chloride. The injections were performed on Dick positive volunteers. The erythrogenic power of the filtrate was such that 0.1 cc. of a 1:100 dilution produced an intense erythema of at least 10 mm. in smallest diameter when the area was examined after twenty and twenty-four hours. Save for the fact that it was much more intense, the erythematous reaction was very similar to the Dick reactions in the various subjects.

The possible antigenic relationship of the staphylococcus and Dick toxins was investigated by attempting to demonstrate the neutralization of the erythrogenic action of staphylococcus filtrate by streptococcus antitoxin. For neutralization experiments Dick positive children were selected who were not, at the time of the tests, suffering from any known infection. Each neutralization test consisted of six simultaneous intracutaneous injections, three into the volar surface of

16. All specimens of blood for culture taken after the institution of chemotherapy were inoculated on mediums enriched with para-aminobenzoic acid.

17. This determination was made for us by Dr. Alvin F. Coburn of the Columbia University College of Physicians and Surgeons, New York.

18. Dick, G. F., and Dick, Gladys H.: Scarlet Fever, Chicago, Year Book Publishers, Inc., 1938, p. 66.

each forearm. Each injection was separated from its neighbor by at least 6 cm., and the reaction was examined under bright daylight eighteen and twenty-four hours after injection. The injections were made as follows:

A. Into the right forearm: (1) 0.1 cc. of a 1:100 dilution of the staphylococcus filtrate incubated for one hour at 37 C. immediately before injection; (2) 0.1 cc. of a 1:10 dilution of the staphylococcus filtrate incubated just prior to injection with nine parts of scarlet fever antitoxin[19] for one hour at 37 C.; (3) 0.1 cc. of a 1:100 dilution of staphylococcus filtrate heated for one hour at 61 C. to test the heat stability of the toxin.

B. Into the left forearm: (1) 0.1 cc. of Dick toxin[20] incubated for one hour at 37 C. immediately before injection; (2) 0.2 cc. of a mixture of equal parts of Dick toxin and scarlet fever antitoxin incubated together for one hour at 37 C.; (3) 0.1 cc. of scarlet fever antitoxin.

In order to carry out satisfactory tests with the staphylococcus toxin, it was necessary to select subjects in whom (1) the Dick reaction remained positive, (2) the erythema of the Dick test was prevented by the previous admixture of the Dick toxin with scarlatinal antiserum and (3) the scarlatinal antiserum itself failed to cause a cutaneous reaction. Ten persons were tested, and 3 suitable subjects were selected in whom the following results were obtained with the staphylococcus filtrate:

1. An intense erythema more than 10 mm. in its least diameter, surrounded by a faint erythematous halo, which blanched readily, resulted from the injection of 0.1 cc. of the 1:100 dilution of the staphylococcus filtrate.

2. In each case there was definite inhibition of the erythema produced by the filtrate when it was incubated with the scarlatinal antiserum before injection. In 1 case neutralization was complete; in the other 2 a faint, blotchy, poorly demarcated erythema could just be discerned.

3. Preheating of the staphylococcus filtrate for one hour at 61 C. completely inactivated the erythrogenic toxin.

## COMMENT

The strain of Staphylococcus aureus which caused the bacteremia and osteomyelitis in the present case has been shown to produce a soluble erythrogenic toxin, the effect of which on the human skin was neutralized by scarlatinal antitoxin. Since, in spite of exhaustive and repeated search, no beta hemolytic streptococci were ever recovered from the patient, it is suggested that the scarlatiniform rash was due to erythrogenic toxin produced by the staphylococcus.[21] Although staphylococcic infection simulating scarlet fever is not common, a review of the literature indicates that there is considerable evidence which points to its being a definite clinical entity.

The study of the staphylococcus toxins by methods analogous to those used in studying the erythrogenic toxin of the hemolytic streptococcus has been reasonably extensive. In 1900 von Lingelsheim[22] described a soluble dermotoxin produced by the staphylococcus, and his observations were soon confirmed by Neisser and Wechsberg[23] and Parker.[24] Pilot and Afremow[25] in 1927, using technics described by the Dicks, obtained a toxic filtrate with which they performed cutaneous tests on human subjects. Intradermal injections of their diluted filtrate produced an erythematous reaction analogous to the Dick test; this reaction was prevented by previous admixture of the filtrate with homologous antitoxin prepared in rabbits. Remé[26] tested fifteen strains of hemolytic Staphylococcus aureus and found that twelve of them elaborated an erythrogenic toxin.

In 1927 Stevens[27] reported 3 cases of clinically "typical" scarlet fever in which the hemolytic staphylococcus was the only pathogenic organism isolated. One of the patients had an acute osteomyelitis of the thigh. Filtrates were prepared for injection into the skin of rabbits, and neutralization tests were carried out with scarlatinal antiserums. It is of interest to note the author's remark that "Three antiscarlatinal serums were tested before one was found which did not contain appreciable amounts of staphylococcus antitoxin." Since the commercial scarlatinal antiserums of that time were prepared with hemolytic streptococcus filtrates, it is probable that neutralization occurred, similar to that previously described. In the same year Satake[28] isolated a strain of hemolytic Staphylococcus aureus from the pharynx of a patient with scarlet fever from whom he had been unable to culture the hemolytic streptococcus. The staphylococcus produced an erythrogenic toxin, and when large doses of the staphylococcus filtrate were administered to patients whose skin reacted to the toxin, a generalized reaction was produced which consisted of prompt fever, malaise, typical scarlatiniform rash, tongue changes, leukocytosis and later desquamation. "It was clear from the results of these experiments," wrote Satake, "that certain strains of staphylococci should cause symptoms very like those of genuine scarlet fever." Clinical reports by numerous later observers[29] have tended to confirm this conclusion.

In 1937 Mundt[30] prepared sterile filtrates from cultures of nineteen strains of hemolytic Staphylococcus aureus isolated from a variety of sources. She performed cutaneous tests with the filtrates on a group of Dick positive subjects, each patient receiving six intracutaneous injections, three in each forearm. In one arm the injections consisted of the usual dose of Dick toxin, the same dose of Dick toxin mixed with an equal amount of scarlatinal antitoxin and the Dick toxin mixed with diphtheria antitoxin. In the other arm a similar set of three injections was made with a dilution of the staphylococcus filtrate in place of the Dick toxin. For a "neutralization" to be recorded, it was required

19. Scarlet fever streptococcus antitoxin prepared by Lederle Laboratories.

20. Scarlet fever streptococcus toxin for the Dick test-Mulford.

21. The elevated titer of antistreptolysins in the patient's serum does not militate against this diagnosis, since the antibodies may represent a response to an earlier unrelated streptococcic infection or may even be accounted for by similarities in the antigenic structure of the hemolysins of the erythrogenic staphylococcus and the usual strains of hemolytic streptococcus. This latter possibility is to be investigated further.

22. von Lingelsheim, W., cited by Neisser, M.: Handbuch der pathogenen Mikroorganismen, ed. 3, Jena, Fischer, 1928, vol. 4, part 1, page 457.

23. Neisser, M., and Wechsberg, F.: Ueber das Staphylotoxin, Ztschr. f. Hyg. u. Infectionskr. **38**: 299, 1901.

24. Parker, T.: Production of an Exotoxin by Certain Strains of Staphylococcus Aureus, J. Exper. Med. **40**: 761, 1924.

25. Pilot, Isadore, and Afremow, M. L.: Studies of Staphylococcus Filtrates: I., J. A. M. A. **89**: 939 (Sept. 17) 1927.

26. Remé, G.: Ueber Hautreaktionen mit Staphylokokkenkulturfiltraten, Ztschr. f. Immunitätsforsch. u. exper. Therap. **69**: 25, 1930.

27. Stevens, F. A.: The Occurrence of Staphylococcus Aureus Infection with a Scarlatiniform Rash, J. A. M. A. **88**: 1957 (June 18) 1927.

28. Satake, T.: Experimental Studies on Scarlet Fever, J. Orient. Med. **6**: 17, 1927.

29. Mackenzie, G. M.: Scarlatiniform Eruption Followed by Desquamation Associated with a Staphylococcus Aureus Bacteremia, in Clinical Miscellany, Springfield, Ill., Charles C Thomas, Publisher, 1934, vol. 1. Zinsser, Enders and Fothergill,[30] page 638. Breen, G. E.: Gangrene in Scarlet Fever, Lancet **2**: 196, 1940. Hippke: Betrachtungen zum Scharlachproblem auf Grund von Beobachtungen in einer militärischen Anstalt, München. med. Wchnschr. **76**: 1873, 1929. Friedemann, U.: Weitere experimentelle und klinische Untersuchungen über den Scharlach V, Ztschr. f. Hyg. u. Infectionskr. **108**: 181, 1928. Kinsella, R. A.; Garcia, D., and Wade, J.: Filtrates from Scarlet Fever and Surgical Hemolytic Streptococcus Infections, Proc. Soc. Exper. Biol. & Med. **24**: 889, 1927.

30. Mundt, M.: Ueber die Neutralisierbarkeit der mit Kulturfiltraten von Staphylokokken erzeugten Hautrötungen mit dem Scharlacheilserum, dissertation, Heidelberg, 1937.

that the following conditions obtain: (1) that there be a definite erythema of more than 0.5 cm. in diameter caused by the staphylococcus and Dick toxins, (2) that the erythema in each instance be prevented by previous admixture of the toxins with scarlatinal antitoxin and (3) that the erythema caused by each toxin be unaffected by previous admixture of the toxin with diphtheria antitoxin. Using these criteria the author found that ten of the nineteen strains of hemolytic Staphylococcus aureus produced a soluble erythrogenic exotoxin, which caused an erythematous reaction in the skin of Dick positive human subjects and was specifically neutralized by previous admixture with scarlatinal antitoxin.

In the following year von Bormann,[31] working in the same laboratory, published an extensive study of erythrogenic toxins contained in filtrates of various bacteria. Among the organisms studied were thirty-eight strains of hemolytic Staphylococcus aureus, a few from cases of scarlet fever but the majority having no known relation to the disease. Seventeen of the thirty-eight strains produced an erythrogenic toxin which could be specifically neutralized by scarlatinal antitoxin prepared with the hemolytic streptococcus. It is of interest to note that the neutralization by commercial staphylococcus antitoxin was less effective than by the scarlatinal antitoxin. An attempt was made to correlate the production of the erythrogenic toxin with that of other staphylococcus toxins, such as hemolysin and leukocidin, but no such correlation was demonstrable. Parallel tests were made with Dick toxin, as a control, on healthy subjects and on patients with early and late stages of scarlet fever. The reaction of the skin to the Dick toxin and to that component of the staphylococcus filtrate neutralized by scarlatinal antitoxin was found to be the same in the two groups of patients.

During the past twenty years there has been a continued broadening of the accepted concept of the pathogenesis of scarlet fever. The original hypothesis that the disease is caused by a single toxin produced by a specific strain of hemolytic streptococcus is no longer tenable. Many strains of beta hemolytic streptococci are now known to possess the power of liberating the causative toxin, and streptococcus toxins of more than one antigenic type are capable of causing the disease. The evidence reviewed in the present report invites a further broadening of the etiologic concept of scarlet fever, for the data presented suggest that a clinical syndrome indistinguishable from scarlet fever may result from infection with certain strains of Staphylococcus aureus. Preliminary immunologic study of the erythrogenic toxin elaborated by the staphylococcus indicates that it is antigenically related to the standard erythrogenic toxin of the hemolytic streptococcus.

SUMMARY

A clinical syndrome indistinguishable from that of scarlet fever and associated with staphylococcic osteomyelitis and bacteremia was observed in a patient from whom no beta hemolytic streptococci could be cultured. The strain of hemolytic Staphylococcus aureus isolated from the patient's blood was found to produce a filtrable erythrogenic toxin which was neutralized by commercial scarlatinal antitoxin. Scarlet fever may occasionally be caused by an erythrogenic toxin produced by certain strains of staphylococci.

31. von Bormann, F.: Dick-Toxin-ähnliches Gift in Filtraten Bouillonkulturen verschiedener Bakterien, Klin. Wchnschr. **17:** 120, 1938.

# ADIE'S SYNDROME

## ITS RECOGNITION AND IMPORTANCE

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The symptom complex of absent tendon reflexes and tonic pupils has been termed Adie's syndrome. Its cause remains unknown. Its importance lies in distinguishing this symptom complex from syphilis of the central nervous system. Neurologists and ophthalmologists are familiar with Adie's syndrome. There have been numerous publications in the literature of those specialties. It seems worth while to call the attention of the general practitioner to this symptom complex, as it is frequently mistaken for syphilis of the central nervous system even in the absence of positive serologic reactions.

The tonic pupil was first described by Saenger [1] in 1902. Markus [2] in 1906 first associated absent tendon reflexes with tonic pupils in a boy of 12 years. The same case was reported by Weber [3] in 1933 after an interval of twenty-seven years. The patient was in good health, with normal offspring, illustrating the benign character of the disorder. Prior to the last decade most reports suggested that this syndrome of absent reflexes and tonic pupils was associated with Argyll Robertson pupils. Moore [4] in 1925 wrote on the nonsyphilitic Argyll Robertson pupil. Holmes [5] and Adie [6] in 1931 called attention to this syndrome, which simulates syphilis of the central nervous system. In 1932 Adie [7] reaffirmed the benign character of this disorder, which has since come to bear his name.

The term tonic pupil is one that requires description so that it may be recognized. A tonic pupil is one having a delayed or slow response to accommodation and convergence. Not only is the response delayed but, in addition, there is an over-response, as shown in the accompanying illustration (case 1). The pupil constricts more than the normal pupil under the same stimulus. This tonic pupil may respond slowly to bright light. The pupil not only constricts gradually but also dilates in the same manner after the stimulus has been withdrawn. The tonic pupil is usually unilateral, although it may be bilateral. The abnormal pupil is usually larger than the normal pupil. This tonic pupil reacts normally to both atropine and physostigmine. It is constricted with acetyl-beta-methylcholine chloride,[8] whereas the unaffected pupil is not constricted. These findings are quite in contrast to the reactions of the Argyll Robertson pupil. With the latter condition the pupils are usually miotic, bilateral and fixed to light stimulation but react promptly to convergence. In the Argyll Robertson pupil there is either a history or both clinical and serologic evidence of

From the Department of Neuropsychiatry, the Lahey Clinic.

1. Saenger, Alfred: Ueber myotonische Pupillenbewegung, Neurol. Centralbl. **21:** 837-839, 1902.
2. Markus, C.: Notes on a Peculiar Pupil Phenomenon in Cases of Partial Iridoplegia, Tr. Ophth. Soc. Med. **26:** 50-58, 1906.
3. Weber, F. P.: Dr. Markus's Original Case of Markus's Syndrome ("Myotonic Pupil" with Absence of Patellar and Achilles Reflexes) Shown 27½ Years Ago, Proc. Roy. Soc. Med. **26:** 530-531, 1933.
4. Moore, R. F.: The Nonluetic Argyll Robertson Pupil, Brit. M. J. **2:** 843-844 (Nov. 7) 1925.
5. Holmes, G.: Partial Iridoplegia Associated with Symptoms of Other Diseases, Tr. Ophth. Soc. U. Kingdom **51:** 209-224, 1932.
6. Adie, W. J.: Argyll Robertson Pupils True and False, Brit. M. J. **2:** 136-138 (July 25) 1931.
7. Adie, W. J.: Tonic Pupils and Absent Tendon Reflexes: A Benign Disorder Sui Generis; Its Complete and Incomplete Forms, Brain **55:** 98-113, 1932.
8. Scheie, H. G.: Site of Disturbance in Adie's Syndrome, Arch. Ophth. **24:** 228-237 (Aug.) 1940.

syphilis, while in Adie's syndrome the history and serologic reactions are negative.

The tendon reflexes most frequently absent in Adie's syndrome are the achilles and patellar reflexes, although all tendon reflexes may be absent. In contrast to tabes dorsalis, the patient with Adie's syndrome has no loss or disturbance of vibratory or position sense, and none of the superficial sensory disturbances, lightning pains or gastric crises seen in tabes dorsalis.

There are variations in Adie's syndrome. Adie[7] believed that there were four phases representing incomplete stages which may go on to the complete form of tonic pupils and absent tendon reflexes. On one end of the scale he placed those patients having tonic pupils alone and on the other end those with absence of reflexes alone. In the intermediate positions he placed those having atypical phases of tonic pupils alone and those having atypical pupils with absence of one or more tendon reflexes. Most neurologists believe it is a mistake to classify patients as having this syndrome who have only absent reflexes. It will be noted in this present series of patients that both the complete and incomplete Adie's syndrome are represented.

## REPORT OF CASES

CASE 1.—A housewife aged 34 was previously told that she had a serious disease, and it was inferred that she had syphilis in spite of repeated negative results of blood and spinal fluid examinations. She became apprehensive and very nervous and complained of fatigue, many aches and pains, sweating and palpitation. She had had a nonvenereal pelvic inflammation following an ectopic pregnancy. The right pupil was larger than the left and constricted slowly to strong light stimulation. There was also a slow constriction with prolonged convergence, the right pupil becoming even smaller than the left. The right pupil dilated slowly. The left pupil reacted normally to light and convergence. Tendon reflexes were generally absent. There was no loss of vibratory or position sense and no cutaneous sensory abnormalities. The patient had only slight complaint referable to her eyes, with blurring on accommodation (figs. 1 and 2).

CASE 2.—A housewife aged 50 had no visual symptoms or complaints. A diagnosis was made originally of tabes dorsalis. There was a general absence of tendon reflexes. The left pupil was larger than the right and irregular and reacted slowly to strong light and convergence. The patient had congenital heart disease with decompensation.

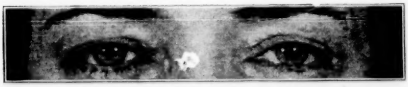

Fig. 1.—Adie's syndrome (case 1). The left pupil is the tonic pupil and is slightly larger than the right; pupils at rest.

CASE 3.—A housewife aged 62 had symptoms of easy fatigue, dizziness, flushing, sweating and loose bowel movements with emotional excitement. There was evidence of mild, generalized arteriosclerosis. The tendon reflexes were generally absent. Vibratory and position sense were intact. The pupils were irregular, the left larger than the right, and they reacted slowly to both strong light and convergence. The right pupil responded normally to light and convergence. There were no symptoms related to the eyes. The patient had roentgenologic evidence of monophasic Paget's disease affecting the skull.

CASE 4.—A salesman aged 41 had always been nervous. He had long-standing functional indigestion, gas and occasional loose bowel movements. He was worried about his heart and showed considerable anxiety. He had a history of alcoholic addiction without psychosis. The right pupil was irregular, larger than the left, and reacted slowly to strong light and to prolonged convergence. The left pupil reacted normally. The tendon reflexes were present and active.

CASE 5.—A man aged 45 had a history of gonorrhea twenty years previously; he denied having syphilis. He complained of "nervous stomach" with attacks of indigestion for five years. He had always been nervous but had had no specific complaints until, following a cold with cough six months previously, dryness of the mouth, loss of sweating, constipation, loss of libido and dizziness developed. The patient had low blood pressure and six months later a typical orthostatic hypotension developed, with dizziness and fainting attacks. Both pupils were irregular and reacted slowly to strong light and prolonged convergence. The tendon reflexes were absent at the knees and ankles. There was no loss of vibratory or position sense.

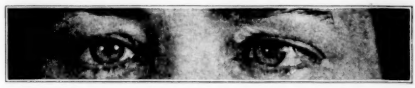

Fig. 2.—Over-response of the left pupil to convergence.

CASE 6.—A housewife aged 53 had had a dilated left pupil for thirty years. In recent years this dilated pupil had constricted. Formerly a diagnosis was made of "burnt out" tabes dorsalis. Both pupils were irregular and apparently fixed to light but reacted slowly to strong light and prolonged convergence. She had a mild photophobia and conjunctivitis. The tendon reflexes at the ankles were absent. The right patellar reflex was more active than the left. The patient was in the menopause. She was very nervous, had hot flashes, fatigue and hypertension, with blood pressure of 160 mm. systolic and 80 mm. diastolic to 190 mm. systolic and 100 mm. diastolic. There was no loss of vibration or position sense.

CASE 7.[9]—A housewife aged 38 had slight blurring of vision with strong light. After her husband's death she became very nervous and had palpitation and lack of emotional control. The patient's father had had a nervous breakdown with depressive symptoms. The right ankle jerk was absent. The remainder of the tendon reflexes were obtained only with reinforcement. The left pupil was larger than the right. The pupils reacted slowly to strong light and prolonged convergence.

CASE 8.[9]—A student aged 14 years was nervous, restless and worried about her health. She had acne of the face. The teacher at school noted that the right pupil was larger than the left and sent the patient for an ophthalmic examination. She had no symptoms referable to the eyes. The right pupil was dilated and larger than the left. It reacted slowly to strong light and prolonged convergence. The right achilles reflex was absent. The other tendon reflexes were present with reinforcement. There was no sensory abnormality. Vibratory and position sense were intact.

## COMMENT

The etiology and pathogenesis of Adie's syndrome remain unknown. The association of this syndrome with other disorders,[10] such as influenza, polyneuritis, encephalitis, multiple sclerosis, orthostatic hypotension, vitamin deficiencies and endocrine disorders, particularly hypothyroidism,[11] has been suggested. In the present series of patients presenting this syndrome, the most frequently met symptoms were nervousness and emotional disorders, with such symptoms as palpitation, sweating and the associated anxiety and fear states. Kennedy and his associates[12] drew attention to the

9. Dr. Davis G. Cogan, Howe Ophthalmological Laboratory, granted the opportunity to examine 2 of these patients (7 and 8).

10. Heersema, P. H., and Moersch, F. P.: Adie's Syndrome, Proc. Staff Meet., Mayo Clin. **14**: 17-22, 1939.

11. Jelliffe, S. E.: The Myotonic Pupil: A Contribution and a Critical Review, J. Neurol. & Psychopath. **13**: 349-358 (April) 1933.

12. Kennedy, Foster; Wortis, Herman; Richard, J. D., and Fair, B. B.: Adie's Syndrome, Arch. Ophth. **19**: 68-80 (Jan.) 1938.

evidence of instability of the autonomic nervous system associated with emotional disturbances in patients with Adie's syndrome, and our series of cases confirms this observation.

Most of the patients with this syndrome consult the physician for entirely different complaints, and the tonic pupils and absent tendon reflexes are found only incidentally in the course of the examination. Symptoms of blurred vision, occasional ocular pain or photophobia may be associated with tonic pupils. Not infrequently the patient's original complaint is lost sight of in the presence of these apparently more ominous findings. Many patients have been told that they have a serious disorder or a syphilitic disorder and have at times been given treatment for syphilis in spite of negative serologic reactions. Although Adie's syndrome when typical is sufficiently characteristic to make a diagnosis, one should not fail to rule out syphilis by complete studies.

Adie's syndrome is a benign disorder and requires no therapy unless it is psychotherapy, particularly if the patients have previously been told that they suffer from syphilis or some serious disorder requiring special treatment.

SUMMARY

Adie's syndrome is a symptom complex with absent tendon reflexes and tonic pupils as the outstanding characteristics. The cause of this syndrome remains unknown. Its importance lies in distinguishing this symptom complex from syphilis of the central nervous system. Tonic pupils may be distinguished from Argyll Robertson pupils. Adie's syndrome is a benign disorder, requiring no special therapy.

## *Clinical Notes, Suggestions and New Instruments*

### HYPERSENSITIVENESS TO A MERCURIAL DIURETIC

#### WITH OBSERVATIONS ON ITS MECHANISM

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Acute toxic reactions following the use of organic mercurials as diuretic agents have received considerable attention in recent publications.[1] The present report deals with an unusual response to these compounds used as diuretics in a case of advanced congestive heart failure. Experiments were performed which throw some light on possible factors that might be involved in the mechanism of this reaction. The observations on our patient cover about five years.

#### REPORT OF CASE

A. G., was an unmarried woman aged 27 when she came under observation. She had rheumatic heart disease, with decided enlargement of the heart, mitral stenosis and insufficiency, auricular fibrillation and an advanced grade of heart failure with congestion.

She appeared to have been hypersensitive to a wide variety of foods which occasionally produced hives. Her history embraced the details commonly encountered in that of a patient with rheumatic heart disease, although there was no history of polyarthritis or chorea. The heart disease was discovered at the age of 10 years, at which time she was confined to bed for about two years with active carditis but without heart failure. The next twelve years, until she was 22, were uneventful. At the end of that period (1933) heart failure began. Up to the present time there have been three episodes of severe failure, for which she was confined to bed. Recovery was not complete from the previous two attacks. She came under our observation during the third attack.

The physical observations during the early period of the last attack of failure were as follows: The patient was frail, weighing 125 pounds (56.7 Kg.). There were severe dyspnea, orthopnea, cyanosis, edema up to the lumbar region, pulmonary rales and ascites. The veins of the neck were distended. The lower edge of the liver was at the level of the umbilicus. There was a systolic murmur over the entire precordium and a rumbling diastolic murmur at the apex. The ventricular rate was 70 a minute. The electrocardiogram showed auricular fibrillation. There was no pulse deficit. The blood pressure was 124 systolic and 66 diastolic. A teleroentgenogram showed decided enlargement of the heart with straight left border.

The laboratory data were not significantly abnormal. There was a trace of albumin in the urine. The urine had a specific gravity of 1.020. There were occasional red blood cells and no white blood cells in the urine. The blood sugar was 103 mg., nonprotein nitrogen 33 mg. and uric acid 8.4 mg. per hundred cubic centimeters. These values were not significantly changed after treatment with the mercurials: blood sugar 85 mg., nonprotein nitrogen 37 mg., uric acid 5.3 mg. and creatinine 1.3 mg. per hundred cubic centimeters. The red blood cell count was 5,376,000, the hemoglobin content 15.2 Gm. and the white blood cell count 8,300, with segmented neutrophils 68 per cent and eosinophils 1 per cent. The red blood cell sedimentation rate was 2 mm. in forty-five minutes. The Kahn and Wassermann reactions of the blood were negative.

Some of the present observations were made while the patient was in bed in the hospital and others when she was ambulant, after being discharged from the hospital. While she was in the hospital a daily record was made of her body weight and the daily water intake and output were charted. The urine was also examined daily, especially for albumin casts and red blood cells. It may be noted at this point that nine daily examinations of the urine during the experiments with the organic mercurials showed no significant changes from the controls before the treatment was started.

The patient received a daily dose of 1½ grains (0.1 Gm.) of digitalis throughout the period of study. This maintained the ventricular rate at a level varying between 70 and 85 a minute except during a period of fever when the ventricular rate rose to 106.

It may also be noted that the use of the mercurial diuretics resulted in a sharp reduction in the signs and symptoms of heart failure, with a loss of 18 pounds (8 Kg.) of edema fluid. She improved sufficiently to become virtually free of symptoms with moderately restricted physical activities.

The unusual reactions produced by the mercurial diuretics in her case became the subject of a special study, which is the point of particular interest in this presentation.

The accompanying chart shows the types of reactions following the organic mercurials. Within less than ten minutes following an intravenous injection of 0.5 cc. of mercupurin there appeared a series of symptoms, which grew in severity during the next twelve hours. The skin became flushed; at times there was a blotching and at other times a diffuse erythema. The conjunctivas became congested. Paresthesias appeared in the skin and mucous membranes with a sensation of "pins and needles" throughout the body, pruritus and numbness of the cheeks and tongue. There was substernal constriction and epigastric pressure, salivation, nausea and vomiting, swelling of the lips, soreness of the mouth and blurring of vision. The vision became so blurred that she was barely able to recognize objects. The temperature rose to 103 F. within seven hours. The blood pressure showed no significant changes. The urine showed no increase of albumin or red blood cells. These symptoms subsided within about seventy-two hours. The severity of the symptoms and their duration varied greatly with the dose and the type of mercurial. In the case of the larger doses, the soreness of the mouth progressed to grayish ulceration, which lasted for as long as eight days.

From the Department of Pharmacology of Cornell University Medical College, New York, the Cardiac Services of the Hospital for Joint Diseases, New York, and Sea View Hospital, Staten Island, N. Y.

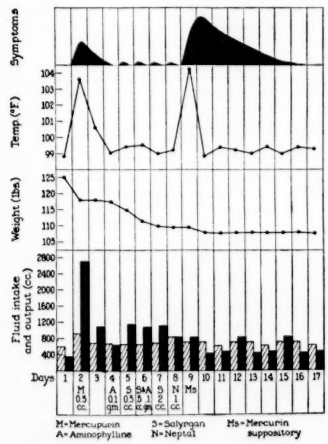
1. Tyson, Mary C.: Danger of Intravenous Mercurial Injections in Nephrosis, J. A. M. A. **117**: 998 (Sept. 20) 1941. Friedfeld, Louis; Kissin, Milton; Modell, Walter, and Sussman, Ralph: Mercupurin (letter to editor), ibid. **117**: 1806 (Nov. 22) 1941.

It may be noted that all the organic mercurials produced some reaction, namely, intravenous mercupurin, salyrgan, neptal and the mercurin suppository. The reaction to salyrgan and neptal was almost negligible, however. In the case of these, there occurred a sensation of "pins and needles" within a few minutes after the injection; vomiting often occurred within a few hours. The temperature did not rise. The patient later prevented the vomiting by taking the injection on an empty stomach and going without food the rest of the day. In the course of time she learned to ignore the slight discomfort produced by the salyrgan. The intravenous mercurpurin or mercurin suppository, however, caused a very severe and dangerous reaction.

Experiments were designed to learn something of the mechanism of the reaction to the mercupurin. It is known that massive diuresis will sometimes cause a severe reaction.[2] Since the first dose produced a diuresis of about 3 liters, this was a possible cause of the reaction. It proved in this case, however, not to be a significant factor, since a similar reaction was caused by mercupurin at a time when the patient was relatively free of edema fluid and no copious diuresis occurred.

Since mercupurin contains some theophylline in solution (about 50 mg. per cubic centimeter), the possibility that the patient might be sensitive to the xanthine content was explored. As may be seen in the chart, however, an intravenous injection of a solution containing 100 mg. of aminophylline alone (about 70 mg. of theophylline) caused no reaction. Such a dose together with 1 cc. of salyrgan also failed to alter the slight reaction caused by salyrgan alone. It is clear, therefore, that the reaction is not caused by the xanthine content of the organic mercurial.

The accompanying table summarizes the results of these and of subsequent experiments. The possibility that the reaction might be due to the fact that the body breaks up the organic compound of mercupurin and liberates more toxic ionizable mercury was studied. Tests were made with other forms of mercury. The results are seen in the table. The patient showed no reaction to an intravenous injection of 20 mg. of the highly ionizable mercury bichloride or to as much as 20 mg. of the poorly ionizable mercuric oxycyanide in 1 per cent solution. These doses represent about four times as much mercury as is present in 0.1 cc. of mercupurin, which caused a rather severe reaction. It is clear, therefore, that the reaction to the mercupurin was not the result of the liberation of ionized mercury. It may be noted that the 20 mg. of mercury bichloride caused a diuresis resulting in a loss of body weight of 3 pounds (1.36 Kg.) in twenty-four hours, or 60 per cent of that following the usual intravenous dose of 2 cc. of salyrgan (80 mg. of mercury).




Types of reactions following organic mercurials.

*Reaction of Patient to Organic Mercurial:*

| Day | Drug | Dose * | Content of Mercury, Mg. | Reaction |
|---|---|---|---|---|
| | 1937 | | | |
| 1 | Salyrgan | 2.0 cc. | 80 | — |
| 4 | Salyrgan | 2.0 cc. | 80 | 1+ |
| 7 | Salyrgan | 2.0 cc. | 80 | 1+ |
| 16 | Mercupurin | 2.0 cc. | 80 | 10+ |
| 28 | Mercurin suppository | 0.5 Gm. | 200 | 10+ |
| | 1938 | | | |
| 2 | Mercupurin | 0.5 cc. | 20 | 5+ |
| 4 | Aminophylline | 0.1 Gm. | .. | 0 |
| 5 | Salyrgan | 0.5 cc. | 20 | 1+ |
| 6 | Salyrgan | 1.0 cc. | 40 | 1+ |
| | Aminophylline | 0.1 Gm. | .. | |
| 7 | Salyrgan | 2.0 cc. | 80 | 1+ |
| 8 | Neptal | 1.0 cc. | 40 | 1+ |
| 9 | Mercurin suppository | 0.5 Gm. | 200 | 10+ |
| 25 | Neptal | 1.5 cc. | 60 | 2+ |
| 32 | Salyrgan | 1.0 cc. | 40 | 1+ |
| 39 | Mercury bichloride | 20.0 mg. | 16 | 0 |
| 43 | Mercuric oxycyanide | 5.0 mg. | 4.3 | 0 |
| 46 | Mercuric oxycyanide | 20.0 mg. | 17 | 0 |
| 53 | Salyrgan | 1.0 cc. | 40 | 1+ |
| 60 | Mercupurin | 0.1 cc. | 4 | 4+ |
| 214 | Histamine | 0.25 mg. | .. | 1+ |
| | Salyrgan | 2.0 cc. | 80 | 1+ |
| | 1938-1942 | | | |
| | Salyrgan | 2.0 cc. (196 weekly doses) | 80 | 1+ |

* All doses were given intravenously except mercurin.

The possibility that the liberation of histamine in the initial allergic reaction to the mercupurin might play a part in the subsequent production of the typical mercury poisoning (ulcerative stomatitis) was tested in one experiment. This hypothesis, however, received no support from the results. A dose of 0.25 mg. of histamine hydrochloride was given subcutaneously. Five minutes later the usual dose of 2 cc. of salyrgan was injected intravenously. Symptoms appeared ten minutes after the histamine injection: flushing of the face, sense of heat and fulness of the head. There was no rise of temperature. These symptoms subsided within an hour. They appeared to be the customary effects of histamine. No intensification of the usual mild salyrgan reaction was apparent. The usual diuresis with loss of 4 pounds (1.8 Kg.) of body weight followed.

The reaction to a cutaneous scratch test for hypersensitiveness to the mercupurin proved negative. The test was made with the full strength ampule solutions of mercupurin and salyrgan on separate areas of the forearm. Isotonic solution of sodium chloride was used for additional control. The observations extended over two hours. A slight elevation appeared at the site of the scratch without itching, erythema or pseudopodia. The scratch with mercupurin was indistinguishable from that with salyrgan.

Severe reactions followed all three doses of mercupurin, even a dose of 0.1 cc. given intravenously. The most severe one followed a dose of 2 cc. intravenously. The patient became desperately ill, and ulceration of the mouth developed, lasting as long as eight days.

The mercurin suppository was used on two occasions. Both times the reactions were as severe as with 2 cc. of mercupurin intravenously.

In the case of salyrgan, more than two hundred injections at weekly intervals were given. The dose was usually 2 cc., containing approximately 80 mg. of mercury. The reaction was negligible.

The hypersensitiveness to the organic mercurial in this patient seemed to remain fixed during a period of years. Her reaction in 1942 was similar to that in 1937.

2. Poll, Daniel, and Stern, J. E.: Untoward Effects of Diuresis with Special Reference to Mercurial Diuretics, Arch. Int. Med. **58**: 1087 (Dec.) 1936.

SUMMARY AND CONCLUSIONS

We have encountered a case of severe hypersensitiveness to mercupurin by intr. venous injection and to mercurin by rectal suppository.

This patient also exhibited a slight toxic reaction to the other mercurial diuretics, but in the case of the others the reaction was negligible.

The continued administration of salyrgan did not result in any appreciable change in the character of the reaction.

The extreme susceptibility to mercupurin was seen from the fact that as little as 0.1 cc., containing only 4 mg. of mercury, produced a severe reaction, with fever, rash, nausea and vomiting, thoracic constriction, paresthesias and swelling of the lips.

This reaction was not related to the degree of diuresis.

The reaction was not due to the liberation of a more toxic ionized mercury. There was no hypersensitiveness to mercury bichloride.

The reaction showed two phases: (1) a nonspecific allergic reaction which came on within a few minutes, namely flushing, a rash and swelling of the lips, and (2) symptoms characteristic of mercury poisoning, namely ulcerative stomatitis. With the smaller doses only the first phase appeared; with the larger doses both were present.

The hypersensitive reaction precluded the use of mercupurin by intravenous injection and of mercurin by rectal suppository. It was not necessary, however, to abandon the mercurials, which were essential in this case for the control of the edema, since salyrgan was tolerated in large doses by intravenous injection with negligible reaction.

## EWING'S TUMOR OF THE SACRUM

### FIVE YEAR SURVIVAL AFTER IRRADIATION

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Ewing's tumor of the sacrum is rarely encountered. In 125 cases of Ewing's tumor reported by Geschickter and Copeland,[1] the neoplasm involved the pelvis in 12, in none of which it occurred in the sacrum, and none of the patients lived over thirteen months. Of the total number of patients, 99 were followed and only 6 survived five years. Brav and Rechtman [2] in 1938 reported a case in which a 10 year old child lived fourteen months with roentgen therapy. They stated that they were unable to find a similar case in the literature.

Malignant tumors of the sacrum include Ewing's tumor, chordoma, myeloma, osteogenic sarcoma and metastatic tumors. The characteristic roentgen appearance is that of a destructive lesion of the sacrum. Because of the diffuse nature of the lesion its destructiveness may not be readily apparent unless the bone density is carefully compared with that of the surrounding pelvis. The final diagnosis depends on the biopsy and the response to therapy. In all cases of Ewing's tumor resection or amputation with irradiation offers the best prognosis for a five year cure.

The patient who is the subject of the present report has survived five years. The case is of interest also because it presents a differential diagnosis in sacral pain and because it emphasizes the importance of palpation of the sacrum as well as of the prostate in rectal examination.

### REPORT OF CASE

J. T., a white man aged 21, was admitted to Tripler General Hospital, Honolulu, T. H., Oct. 10, 1936 with sacral pain of one month's duration which had gradually increased in severity. The pain was most severe on flexion and extension of the spine and was especially severe at night. The patient's general health was good, and he had no other complaints except increasing constipation and slight urinary difficulty during the previous two weeks. He was ambulatory and afebrile. His normal weight was 144 pounds (65 Kg.) and the present weight

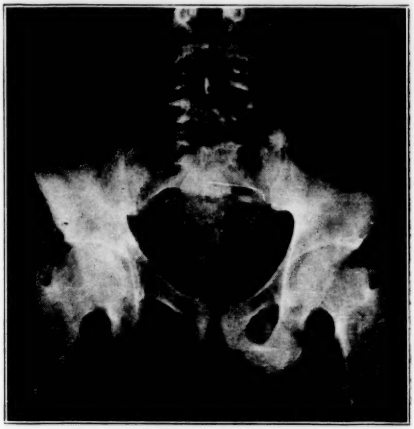


Fig. 1.—Decreased density in the sacrum on Nov. 22, 1936, two and one-half months after onset of symptoms.

was 127 pounds (57.6 Kg.). The special senses, the abdomen, heart and lungs were normal. There was no adenopathy. The blood pressure was 128 mm. of mercury systolic and 78 mm.

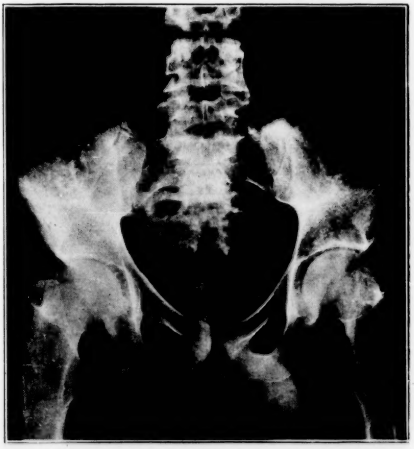


Fig. 2.—Appearance on May 24, 1937, after operative removal of coccyx and roentgen therapy. The sacrum has normal density.

diastolic. Serologic examination gave negative results. Rectal examination revealed no tenderness or enlargement of the prostate, and no mass was discovered. The nervous system and the extremities were normal, and there was no sciatic radiation of pain. The patient walked cautiously because of pain. Roentgen

From Lawson General Hospital and Walter Reed General Hospital.

1. Geschickter, C. F., and Copeland M. M.: Tumors of Bone revised ed., New York, American Journal of Cancer, 1936.

2. Brav, E. A., and Rechtman, A. M.: Primary Endotheliomyeloma (Ewing's Tumor) of the Sacrum, J. Bone & Joint Surg. **20**: 1034 (Oct.) 1938.

examination showed sacralization of the right fifth transverse process, and there was haziness in the right sacroiliac joint.

On November 15 he first noticed impaired sensation in the genital region. The second rectal examination revealed a large, firm, circumscribed tumor mass, 10 cm. in diameter, in the hollow of the sacrum and weakness of the sphincter. On November 23 aspiration of the tumor mass was attempted under local anesthesia to rule out abscess formation, but no pus was obtained.

Fig. 3.—Lateral view of the sacrum on Oct. 24, 1939, three years after admission.

On December 9, under spinal anesthesia with 150 mg. of procaine hydrochloride, a posterior incision was made with removal of the coccyx. There was a gush of necrotic hemorrhagic material from a large cavity in the region of the sacrum. This cavity contained fragments of bone, tumor tissue and clotted blood. The cavity was packed, and the wound was partially closed. The clinical diagnosis was sarcoma of the sacrum. Rectal examination immediately after operation showed no decrease in the size of the mass. Diagnosis on frozen section was sarcoma; on the basis of the fixed specimen it was Ewing's tumor.

This case is carried by the Bone Tumor Registry under number 2319 (diagnosis: 3. Ewing's sarcoma. 2. Reticulum cell sarcoma). The following description of the microscopic picture of the tumor (accession 528630) is furnished by Col. J. E. Ash, curator of the Army Medical Museum:

"Microscopic examination showed small fragments of cancellous bone, the spaces of which were filled with cell masses of the reticulum cell type. The cell nuclei were uniform, oval and slightly irregular in contour. The nucleoli were small. The cell outlines were indistinct. No intercellular substance was identified. The neoplastic cells were seen invading the fibrous stroma. The diagnosis of Ewing's tumor was made."

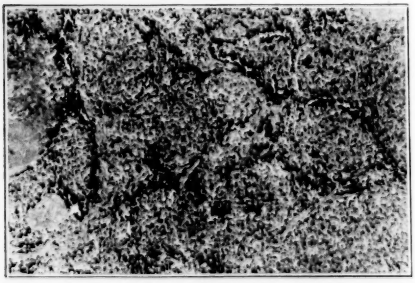


Fig. 4.—Section of tumor under low power.

High voltage roentgen therapy was started immediately. The packing was completely removed on the tenth day, and the wound quickly healed. The patient had complete relief of pain soon after operation and roentgen therapy. Rectal examination on December 30 showed that the mass was softer but was still the same size. Roentgen examination now showed considerable destruction of the sacrum. The chest did not show metastasis. Rectal examination on Jan. 11, 1937, one month after operation and roentgen therapy, showed a substantial decrease in size of the tumor. The patient received a total of 7,000 roentgens (1,400 roentgens to each of five ports).

He was returned to the United States and was admitted to Walter Reed General Hospital, Washington, D. C., on February 20. Physical examination at that time gave essentially negative results. Roentgenograms showed absence of the coccyx and of the destructive lesion involving the lower portion of the sacrum, which had been more extensive on the right side. Complete genitourinary study showed no pathologic condition. Two further courses of roentgen treatment were given, with a total of 4,611 and 2,522 roentgens respectively. He was returned to duty on September 24 and was subsequently discharged from the Army on expiration of enlistment without apparent disability.

### FOLLOW-UP EXAMINATION

The patient returned for follow-up examinations at the orthopedic clinic of Walter Reed General Hospital on June 20, 1938, Oct. 24, 1939 and Oct. 6, 1941. He has remained in excellent health, and no evidence of local or metastatic involvement has been discovered by rectal examination and roentgen examination of the chest and pelvis. On the last visit he weighed 148 pounds (67 Kg.) and was working as a machinist in a navy yard.

### SUMMARY

In an unusual case of Ewing's tumor of the sacrum, five year survival followed biopsy and intensive roentgen therapy.

## CHRONIC PULMONARY CHANGES AND BRONCHIAL ULCERATION IN AN ELECTRIC ARC WELDER

H. R. NAYER, M.D., NEW YORK

In 1936 Doig and McLaughlin [1] first described chronic roentgenographic changes in the lung fields of 16 arc welders. Subsequently Enzer and Sander [2] and Sander [3] reported similar findings in 10 of 26 welders examined. The roentgenographic abnormalities, discovered by surveys on apparently healthy workers, ranged from increased hilar shadows to a generalized fine or nodular mottling simulating silicosis. In all cases silicosis could be ruled out by the occupational history. The workers had no symptoms and were not disabled in any way. There was a history of long exposure to the products of arc welding, usually fifteen years or more. Those arc welders who showed pulmonary changes had, at some time, worked in a confined or poorly ventilated space for at least two years. Autopsy on one man who died in an accident revealed extensive intracellular deposition of iron pigment in the lungs and tracheobronchial nodes. There was no evidence of any reaction to the iron.[2] The roentgenographic changes were apparently produced simply by the accumulation of the iron pigment.

Electric arc welding is a method of fusing metals in which an arc is sustained between a metal electrode and the material to be welded. During the procedure the electrode is consumed and forms the filler material; it is therefore common practice to use electrodes of a composition similar to that of the metal to be subjected to welding. The commonly used mild steel electrode consists of approximately 99 per cent ferrous material with minute amounts of such alloy substances as carbon, manganese, phosphorus, silicon and nickel. At present the trend

From the Medical Service of Dr. A. A. Epstein, Beth Israel Hospital. Dr. M. L. Som gave permission to report this case and Dr. Harry Wessler gave helpful suggestions.

1. Doig, A. T., and McLaughlin, A. I. G.: X-Ray Appearances of the Lungs of Electric Arc Welders, Lancet **1**: 771 (April 4) 1936.
2. Enzer, Norbert, and Sander, O. A.: Chronic Lung Changes in Electric Arc Welders, J. Indust. Hyg. & Toxicol. **20**: 333 (May) 1938.
3. Sander, O. A.: Respiratory Hazards of Electric Arc Welding, Indust. Med. **8**: 177 (May) 1939.

is to use coated electrodes, which are more efficient. The coating produces a gas shield which prevents contact of the atmosphere with the molten metal. The coated rods also produce more heat and prevent heat loss. Many coatings are secret trade formulas, but it is known that they are composed of various materials, such as fluorides, silicates, borates, aluminum and chromium. Fumes arising from coated rods are largely inorganic material consisting of finely divided iron oxide; the average particle is less than 0.5 millimicron.[4] Observations on animals exposed to the fumes of arc welding with uncoated electrodes reveal evidence of iron deposition in the lungs with transportation of this material to the periphery of the lungs and to the tracheobronchial lymph nodes.[5]

The clinical literature on these chronic pulmonary changes remains relatively sparse, and case reports are few. In view of the importance of arc welding, particularly in this period of industrial expansion, this subject merits further attention. Furthermore, the case to be reported presented several unusual features some of which have not been previously described.

## REPORT OF CASE

*History.*—A. K., a white man aged 30, admitted to the hospital on April 10, 1941, complained of cough and difficulty in breathing of one year's duration. About one year before admission he had noted the gradual onset of dyspnea, progressing in severity and increasing with effort. At the same time he began to cough and expectorated moderate amounts of tenacious, nonfoul, whitish sputum. His symptoms increased and the sputum became purulent. There had been no chest pain or hemoptysis, and his general condition remained fairly good.

*Occupational History.*—He had worked steadily as an electric arc welder for the past seven years. All his work was in building and ship construction, and he had worked with ordinary structural steel using coated electrodes. In accordance with the general practice, he had worn the welder's helmet, which protects against injury from heat and light but does not prevent the inhalation of fumes. As far as he could recall, these fumes had not produced any symptoms in him or his fellow workers.

Unfortunately, during his hospital stay no data were elicited with regard to work in poorly ventilated spaces. His most recent work had been in ship building, and it is probable that some of this welding had been carried out in poorly ventilated surroundings.

*Physical Examination.*—On admission he was afebrile. He was moderately dyspneic at rest; there was no orthopnea or cyanosis. The trachea was deviated to the right and was freely movable. The fingers were not clubbed. A persistent rhonchus was heard over the right lung in addition to inconstant rhonchi scattered over both lungs. There was a short systolic blow over the apex. The remainder of the physical examination disclosed no abnormalities.

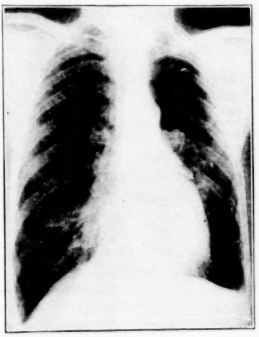
*Laboratory Data.*—The hemoglobin amounted to 95 per cent (Sahli). The red blood cells numbered 4.4 million and the white blood cells 8,100, with a normal differential count. The Wassermann reaction of the blood was negative. The urine was normal. Sputum cultures showed a variety of organisms, including Staphylococcus albus and hemolytic and nonhemolytic streptococci.

*Course in the Hospital.*—The admission roentgenogram showed multiple linear and nodular densities traversing the middle third of the right lung from the root out to the periphery. There was also some exaggeration of the linear markings of the left lung, as shown in the accompanying illustration. The tentative diagnosis, on admission, was bronchogenic carcinoma with lymphangitic spread.

Bronchoscopy (Dr. M. L. Som) four days after admission revealed a considerable amount of purulent material in the lower part of the trachea. The tracheal bifurcation was distorted so that the lumen of the left main bronchus was narrowed and could not be entered. There was an ulcerated granulating lesion on the anterior wall of the right main bronchus just below the bifurcation; a large amount of nonfoul purulent secretion was seen distal to this lesion. Sections of this granulation tissue, removed by biopsy, showed nonspecific inflammatory changes with large masses of iron pigment scattered about. The pus from the bronchi was studied for fungi, with negative results.

In order to relieve the patient's obstructive symptoms, the bronchoscopist decided to remove the granulation tissue from the right side and to dilate the left main bronchus. Accordingly, bronchoscopy was done on five further occasions during the patient's hospital stay of approximately one month. Three further specimens from the lesion in the right main bronchus showed nonspecific inflammation and fibrosis with large masses of iron pigment. The left main bronchus was dilated to a diameter of about 9 mm. so that the bronchoscope could be passed beyond. During the sixth and last bronchoscopy, two days before the patient's discharge, no ulcer was seen and the right main bronchus appeared normal; the lumen of the left main bronchus was now widely patent.

Following the fifth bronchoscopy there was a short period of massive collapse of the left lung, apparently caused by a mucous plug. Aside from this episode, the patient's course was satisfactory. His dyspnea and cough were greatly relieved and his general condition improved. Roentgenograms of the chest throughout were unchanged. He was discharged on May 17, 1941 and returned to work.



Linear and nodular densities throughout the right lung on admission. There are also some infiltrations in the region of the left hilus and increased markings in the middle third of the left lung.

When last seen by his private physician on Oct. 11, 1941 [6] he was still bringing up some purulent sputum. He was working and had gained 13 pounds (6 Kg.), and his general condition was fairly good. A roentgenogram of the chest showed no change as compared with changes of May 1941.

## COMMENT

On the basis of the occupational history and roentgenographic findings in the chest this patient can be classified as an electric arc welder with chronic pulmonary changes, in the same category with the cases previously described in the literature. He presented, however, several unusual features. He had been an arc welder for seven years; in the other cases reported in which the time spent in this occupation has been noted, the average exposure has been eighteen years. In contrast to the absence of symptoms hitherto noted, this man suffered from cough, sputum and dyspnea. These symptoms seem to have been produced primarily by the bronchial involvement, with resulting distal infection; they cleared to a considerable degree when the bronchial obstruction was relieved.

Bronchial lesions accompanying chronic pulmonary changes in electric arc welders have not been previously reported. The mechanism whereby these bronchial changes were produced is not clear. Whether these were due to irritation by one or more of the alloy substances present in the steel, such as chromium and phosphorus, by pressure of enlarged lymph nodes or by some other mechanism cannot be stated. I simply wish to call attention to this involvement of the major bronchi in an arc welder in the hope that further observations may help to clarify the problem.

575 West End Avenue.

4. Britten, J. A., and Walsh, E. L.: Health Hazards of Electric and Gas Welding, J. Indust. Hyg. & Toxicol. **22**: 125 (April) 1940.

5. Harrold, G. C.; Meek, S. F., and McCord, C. P.: A Chemical and Physiologic Investigation of Electric Arc Welding, J. Indust. Hyg. & Toxicol. **22**: 347 (Oct.) 1940.

6. Jaffin, A. E.: Personal communication to the author.

## ACUTE AGRANULOCYTOSIS FOLLOWING SULFADIAZINE

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Assistant Resident in Medicine, Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals

Toxic symptoms following the use of sulfadiazine in comparison with those following the other sulfonamides are mild and infrequent.

A decrease in the leukocyte count below 5,000 per cubic millimeter of blood with or without a decrease in the granulocytes occurs not uncommonly during the course of sulfanilamide and less often during sulfapyridine and sulfathiazole therapy.[1]

Leukopenia following sulfadiazine administration has been observed. In a total of 776 cases[2] the incidence was 1.67 per cent. Keefer[1] reports an incidence of 2 per cent.

Acute agranulocytosis occurring after sulfadiazine therapy has not been reported. For this reason it was felt that the following case should be recorded.

### REPORT OF CASE

A white woman aged 41, married, entered the medical wards of the Boston City Hospital on Sept. 24, 1941 because of jaundice of five days' duration.

*Laboratory Studies of Blood During Period of Hospitalization*

| Date | Red Blood Cells, Million | Hemoglobin, per Cent | White Blood Cells | Sulfadiazine | | Icterus Index |
|---|---|---|---|---|---|---|
| | | | | Total | Free | |
| 9/25 | 4.49 | 82 | 10,550 | ..... | ..... | 110 |
| 9/30 | ..... | .... | 6,250 | ..... | ..... | 60 |
| 10/ 4 | ..... | 70 | 8,200 | ..... | ..... | 40 |
| 10/ 7 | ..... | .... | ..... | 5.7 | 4.6 | 40 |
| 10/10 | ..... | .... | ..... | 9.2 | 9.2 | ..... |
| 10/16 | ..... | .... | ..... | 12.8 | 11.4 | 30 |
| 10/18 | 3.41 | 65 | ..... | ..... | ..... | ..... |
| 10/22 | ..... | 69 | 5,000 | ..... | ..... | ..... |
| 10/24 | ..... | .... | ..... | 20.4 | 16.8 | 18 |
| 10/27 | ..... | .... | 4,300 | ..... | ..... | ..... |
| 10/29 | ..... | 62 | 650 | 28.3 | 25.6 | ..... |
| 10/30 | ..... | 69 | 1,000 | 18.7 | 16.3 | 12 |
| 10/31 | 3.40 | 74 | 3,200 | 4.4 | 3.9 | ..... |
| 11/ 3 | ..... | .... | 3,600 | ..... | ..... | ..... |
| 11/ 6 | ..... | .... | 3,700 | ..... | ..... | ..... |
| 11/ 9 | ..... | 60 | 4,600 | ..... | ..... | ..... |
| 11/17 | ..... | 72 | 5,500 | ..... | ..... | 12 |

The present illness began about two weeks previously with an episode of nausea and vomiting which persisted for five days. This was followed by prolonged nausea and anorexia. She had been taking moderate amounts of alcoholic beverages daily for the past two years. Simultaneously with the onset of jaundice she noted dark colored urine. She never noticed clay colored or tarry stools, although on occasions they were streaked with bright red blood. She had no abdominal pain, loss of weight or pruritus and no intolerance to fried or fatty foods.

On admission to the hospital her oral temperature was 101.6 F., the pulse rate 100 and the respiratory rate 30 a minute.

The patient was well developed, well nourished, jaundiced and moderately ill. There were a few scattered, fine telangiectases over the face. The pupils were normal and the scleras icteric. The chest was resonant on percussion and no rales were heard. The heart was not enlarged, the rhythm was regular and there was a grade 1 systolic murmur at the fourth left interspace close to the sternum. The blood pressure was recorded as 116 millimeters of mercury systolic and 74 diastolic. The abdomen was soft. The liver edge was easily palpable 4 cm. below the right costal margin, and the surface was smooth and nontender. The spleen could not be felt. Rectal examination revealed external and internal hemorrhoids.

Laboratory work showed that the red blood cell count was 4,490,000 and the white blood cell count 10,550 per cubic millimeter of blood. The hemoglobin concentration was 82 per cent (Sahli). The differential smear revealed 63 per cent polymorphonuclear leukocytes, 16 per cent stab forms, 9 per cent lymphocytes, 4 per cent large lymphocytes and 8 per cent monocytes. The red blood cells and platelets appeared normal in the smear. The Hinton test on the blood serum gave a negative reaction. The blood nonprotein nitrogen was 29 mg. per hundred cubic centimeters and the icterus index 110. The blood prothrombin time was 100 per cent of normal. The hippuric acid excretion test yielded no hippuric acid. The total protein of the blood serum was 5.5 Gm. per hundred cubic centimeters of blood, with the albumin and globulin fractions 2.7 Gm. and 2.8 Gm. respectively. The alcohol-iodine test for bile in the urine was strongly positive, and the urobilinogen test was positive in a dilution of 1:32.

A diagnosis of portal cirrhosis with acute hepatitis was made. The patient was treated with a high carbohydrate, high protein, low fat diet with parenteral vitamins. During the following nine days she improved, with the icteric index dropping to 60. The hemoglobin concentration in the blood was 70 per cent and the leukocyte count 8,200 per cubic millimeter of blood. The temperature curve was intermittently as high as 101 F.

Sulfadiazine was administered on October 3 because of fever and roentgen findings of bronchopneumonia. Two Gm. of the drug was given by mouth and then 1 Gm. every four hours. Ten days later the drug was discontinued but inadvertently begun again the following day. The laboratory studies at this time are shown in the accompanying table. The icterus index dropped to 18. The hippuric acid excretion test yielded 2.1 Gm. of hippuric acid. The bromsulphalein excretion test showed 25 per cent retention at the end of fifteen minutes. The daily urinary output was more than 1,000 cc.

On the twenty-fourth day of chemotherapy the temperature rose to 102 F. The patient became nauseated and vomited. The following day it was discovered that the sulfadiazine had been continued and administration of it was stopped. The blood hemoglobin concentration was 62 per cent. The leukocyte count was 650 per cubic millimeter of blood. A differential smear revealed no polymorphonuclear leukocytes. This smear was reviewed at the Thorndike Memorial Laboratory and the differential count was reported as 1 basophil, 4 small lymphocytes, 7 large lymphocytes, 1 young lymphocyte, 14 monocytes and 12 young monocytes.

She was given 500 cc. of citrated whole blood by vein and 10 cc. of pentnucleotide intramuscularly. The following day the leukocyte count was 1,000 per cubic millimeter of blood, and the differential smear showed 4 per cent stab forms, 1 per cent myelocytes, 10 per cent small lymphocytes, 29 per cent large lymphocytes, 2 per cent young lymphocytes, 2 per cent atypical lymphocytes, 35 per cent monocytes, 12 per cent young monocytes and 5 per cent clasmatocytes. An additional 500 cc. of citrated whole blood was given, following which the leukocyte count rose to 3,200 per cubic millimeter of blood and the differential smear showed 17 per cent polymorphonuclear leukocytes, 31 per cent stab forms, 25 per cent small lymphocytes, 6 per cent large lymphocytes, 18 per cent monocytes, 2 per cent metamyelocytes and 1 per cent myelocytes.

At the time of the toxic reaction it may be seen from the table that the blood sulfadiazine concentration[3] was high. There was no change in the icterus index. The alcohol-iodine test for bile in the urine was negative, and the urobilinogen test was positive in a dilution of 1:6.

There was no untoward reaction from the transfusions, and two days later the temperature dropped to normal. The leuko-

From the Third Medical Service (Tufts) and the Boston City Hospital.

1. Keefer, C. S.: Toxic Reactions Following Sulfonamides, New England J. Med. **226:** 226 (Feb. 12) 1942.

2. Finland, Maxwell; Strauss, Elias, and Peterson, O. L.: Sulfadiazine: Therapeutic Evaluation and Toxic Effects on 446 Patients, J. A. M. A. **116:** 2641 (June 14) 1941. Flippin, H. F.; Rose, S. B.; Schwartz, Leon, and Domm, A. H.: Sulfadiazine and Sulfathiazole in the Treatment of Pneumococcic Pneumonia: A Progress Report on 200 Cases, Am. J. M. Sc. **201:** 585 (April) 1941. Trevett, G. I.; Nelson, R. A., and Long, P. H.: Studies on Sulfadiazine, Bull. Johns Hopkins Hosp. **69:** 303 (Oct.) 1941. Billings, F. T., Jr., and Wood, W. B., Jr.: Studies on Sulfadiazine, ibid., p. 314.

3. Miss Alice Ballou of the Thorndike Memorial Laboratory determined concentrations of sulfadiazine in the blood.

cyte count continued in the vicinity of 4,000 per cubic millimeter of blood and was 5,500 at the time of discharge from the hospital fifty-seven days after admission.

SUMMARY

The case of acute agranulocytosis following sulfadiazine therapy reported here is of interest in that the toxic reaction appeared only with prolonged administration of the drug in therapeutic doses and at a time when the blood concentration of sulfadiazine was high.

Treatment consisted of stopping the drug and of administering pentnucleotide and giving blood transfusions. Following this therapy the patient made an uneventful recovery.

78 East Concord Street.

## *Special Article*

# DIPHTHERIA MORTALITY IN LARGE CITIES OF THE UNITED STATES IN 1941

NINETEENTH ANNUAL REPORT

The procedure followed in obtaining data for this report has been described in the review of typhoid mortality for these same cities.[1] Briefly, a communication was addressed to the health officer of each of the cities,

TABLE 1.—*Death Rates of Fourteen Cities in New England States from Diphtheria (Including Croup) per Hundred Thousand of Population*

| | 1941 | 1940 | 1935-1939 | 1930-1934 | 1925-1929 | 1920-1924 | 1915-1919 | 1910-1914 | 1905-1909 | 1900-1904 | 1895-1899 | 1890-1894 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| New Haven | 0.0 | 0.0 | 0.4* | 0.7† | 1.6 | 7.1 | 14.2 | 14.9 | 22.7 | 15.6 | 54.8 | 74.5 |
| Lynn | 0.0 | 0.0 | 0.4 | 4.7 | 13.5 | 17.0 | 17.8 | 17.2 | 21.7 | 38.0 | 44.0 | 49.0 |
| New Bedford | 0.0 | 0.0 | 0.4 | 5.0 | 10.9 | 16.5 | 17.0 | 20.9 | 22.6 | 25.1 | 53.6 | 29.0 |
| Somerville | 0.0 | 0.0 | 0.4 | 3.3 | 5.7 | 19.7 | 30.2 | 21.4 | 21.3 | 40.5 | 57.8 | 37.4 |
| Waterbury | 0.0 | 0.0 | 1.4 | 2.4 | 2.6 | 17.9 | 23.0 | 29.6 | .... | .... | .... | .... |
| Cambridge | 0.0 | 0.0 | 0.3 | 1.2 | 3.2 | 8.9 | 12.9 | 23.8 | 25.3 | 46.7 | 71.9 | 58.0 |
| Worcester | 0.0 | 0.0 | 0.7‡ | 3.3† | 8.6 | 15.5 | 14.1 | 21.3 | 32.2 | 16.5 | 50.3 | 45.8 |
| Bridgeport | 0.0 | 0.0 | 0.8 | 1.2 | 11.8 | 19.6 | 22.4 | 23.3 | 26.8 | 34.2 | 63.9 | 79.3 |
| Hartford | 0.0 | 0.6 | 1.9† | 1.1† | 5.3 | 11.9 | 14.8 | 25.3 | 28.1 | 38.8 | 47.8 | 120.9 |
| Boston | 0.4† | 0.3† | 0.7‡ | 3.2† | 8.3 | 20.2 | 26.3 | 20.0 | 26.2 | 53.7 | 83.9 | 112.2 |
| Providence | 0.4 | 0.8* | 0.6† | 5.1 | 9.5 | 15.8 | 29.3 | 26.8 | 30.7 | 41.2 | 53.5 | 55.3 |
| Springfield | 1.3 | 0.0 | 0.3* | 2.1 | 10.3 | 15.4 | 24.9 | 19.1 | 31.3 | 29.6 | 51.3 | 68.2 |
| Lowell | 1.9 | 0.0 | 2.8 | 9.4 | 10.6 | 16.7 | 25.3 | 29.6 | 31.0 | 59.3 | 44.3 | 36.4 |
| Fall River | 2.6 | 0.9 | 2.4 | 3.6 | 12.0 | 25.5 | 33.6 | 24.0 | 34.4 | 50.1 | 43.8 | 46.9 |

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.

requesting the number of deaths from diphtheria both among residents and among nonresidents which were recorded in 1941. In calculating death rates the 1940 census figures were used. The practice of charging all deaths, both among residents and among nonresidents, against the individual city has been continued with the inclusion of appropriate symbols similar to those employed in previous years. Such symbols indicate those cities in which either (1) all diphtheria deaths were stated to be in nonresidents or (2) one third or more of such deaths were stated to be in nonresidents. Attention is directed to tables 11 and 13, which together list forty-five cities which record no diphtheria deaths among residents in 1941. In addition to the twenty cities (table 12) with no diphtheria and typhoid deaths in 1941, eleven cities (Albany, Columbus, Dayton, Kansas City, Kan., Knoxville, Memphis, Nashville, St. Paul, Syracuse, Toledo, Youngstown) report no death among residents from either cause.

The fourteen New England cities (table 1) report nearly double the number of deaths recorded in the preceding year (eleven in 1941, six in 1940). The death rate for the group as a whole has increased from 0.23 in 1940 to 0.43 in 1941 and these cities now trail not only the Middle Atlantic group (0.17), which has held first place for several years, but also the West North Central group (0.18). The increase in number of deaths has been confined to three cities (Fall River, Lowell, Springfield). Nine cities (Bridgeport, Cambridge, Hartford, Lynn, New Bedford, New Haven, Somerville, Worcester, Waterbury) record no death (there were ten in 1940, seven in 1939). It is stated that there has occurred no death from diphtheria in Lynn for five years, none in New Bedford and New Haven for four years, none in Somerville and Waterbury for three years. Lynn reports no diphtheria or typhoid death during the past five years, New Bedford none for four years. Boston records three diphtheria deaths for 1941, two among residents. Providence reports one death among residents, making only the second such death during the last six years. After a lapse of three years with no death and four years without a death among residents, Lowell records two deaths

TABLE 2.—*Death Rates of Eighteen Cities in Middle Atlantic States from Diphtheria (Including Croup) per Hundred Thousand of Population*

| | 1941 | 1940 | 1935-1939 | 1930-1934 | 1925-1929 | 1920-1924 | 1915-1919 | 1910-1914 | 1905-1909 | 1900-1904 | 1895-1899 | 1890-1894 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Rochester | 0.0 | 0.0 | 0.0 | 0.7 | 7.5 | 16.9 | 12.7 | 22.1 | 32.4 | 32.3 | 45.9 | 96.6 |
| Elizabeth | 0.0 | 0.0 | 0.5† | 4.5 | 13.2 | 19.2 | 19.3 | 14.8 | 51.7 | 42.4 | 60.5 | 79.3 |
| Yonkers | 0.0 | 0.0 | 0.3 | 0.6 | 10.4 | 17.0 | 17.7 | 25.3 | .... | .... | .... | .... |
| Trenton | 0.0 | 0.0 | 0.8 | 2.7 | 4.4 | 7.3 | 8.8 | 12.8 | 15.8 | 23.6 | 92.1‖ | 89.7‖ |
| Newark | 0.0 | 0.0 | 0.2 | 3.0 | 14.5 | 9.7 | 14.6 | 23.3 | 30.1 | 46.7 | 79.1 | 110.4 |
| Syracuse | 0.0 | 0.0 | 0.2† | 0.4† | 2.0 | 22.9 | 12.9 | 16.6 | 17.4 | 17.7 | 31.1 | 55.4 |
| Camden | 0.0 | 0.0 | 2.7 | 8.1† | 21.9 | 20.3 | 23.2 | 38.8 | 48.9 | 52.6 | 93.8 | 194.0 |
| Buffalo | 0.0 | 0.2 | 0.8† | 4.9 | 9.1 | 24.0 | 27.3 | 22.0 | 18.4 | 24.8 | 53.5 | 60.9 |
| Scranton | 0.0 | 0.7§ | 0.7 | 1.7 | 11.7 | 12.3 | 22.1 | 23.4 | .... | .... | 77.8‖ | 48.6‖ |
| Reading | 0.0 | 0.9 | 2.5 | 3.6 | 7.3 | 21.1 | 16.9 | 35.7 | 29.2 | 70.1 | 72.0 | 94.1 |
| New York | 0.1 | 0.1 | 0.6 | 2.2 | 10.7 | 14.0 | 21.8 | 28.0 | 40.0 | 58.0 | 85.8 | 134.4 |
| Pittsburgh | 0.1 | 0.7 | 1.3 | 5.1 | 11.5 | 20.1 | 22.3 | 29.3 | 29.4 | 30.9 | 32.9 | 86.4 |
| Philadelphia | 0.2† | 0.0 | 0.5 | 1.3 | 11.8 | 16.7 | 22.7 | 24.6 | 34.1 | 50.0 | 100.6 | 119.4 |
| Paterson | 0.7 | 0.0 | 0.9 | 6.3 | 9.1 | 18.5 | 13.5 | 16.1 | 25.5 | 52.9 | 111.8 | 145.4 |
| Erie | 0.9 | 0.0 | 0.0 | 4.0 | 5.8 | 16.8 | 15.1 | 17.7 | 27.1 | 42.3 | 23.1 | .... |
| Utica | 1.0 | 0.0 | 0.0 | 1.2 | 13.4‡ | .... | .... | .... | .... | .... | .... | .... |
| Jersey City | 1.0 | 2.6 | 2.4 | 6.0 | 11.5 | 18.4 | 21.0 | 23.2 | 32.6 | 57.9 | 85.4 | 108.6 |
| Albany | 1.5* | 0.0 | 0.2* | 3.0 | 7.5 | 12.8 | 10.4 | 20.0 | 31.6 | 26.9 | .... | .... |

*All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‡ Diphtheria deaths from Chapin's Municipal Sanitation.
‡ Incomplete data.
¶ Diphtheria data furnished by Pennsylvania Department of Health, Harrisburg.

TABLE 3.—*Death Rates of Ten Cities in South Atlantic States from Diphtheria (Including Croup) per Hundred Thousand of Population*

| | 1941 | 1940 | 1935-1939 | 1930-1934 | 1925-1929 | 1920-1924 | 1915-1919 | 1910-1914 | 1905-1909 | 1900-1904 | 1895-1899 | 1890-1894 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Miami | 0.0 | 0.0 | 2.2† | 2.5 | 5.4‡ | .... | .... | .... | .... | .... | .... | .... |
| Charlotte | 0.0 | 2.0† | 6.0† | 4.1 | .... | .... | .... | .... | .... | .... | .... | .... |
| Washington | 0.3† | 0.5 | 2.8 | 3.7 | 7.1 | 10.5 | 11.9 | 6.9 | 11.2 | 23.5 | 50.9 | 77.9 |
| Baltimore | 0.6† | 0.3† | 1.0† | 1.7 | 7.6 | 11.4 | 13.5 | 14.2 | 16.1 | 33.0 | 68.1 | 70.0 |
| Wilmington | 0.9 | 0.0 | 1.6 | 6.2 | 10.9 | 11.6 | 15.2 | 18.0 | 27.8 | 50.9 | 84.9 | 83.8 |
| Richmond | 1.0 | 1.0† | 1.7† | 3.3† | 6.9 | 9.8 | 5.8 | 7.0 | 9.8 | 24.4 | 17.6 | 59.7 |
| Jacksonville | 1.7 | 1.7† | 2.4 | 5.5 | 6.3‡ | .... | .... | .... | .... | .... | .... | .... |
| Tampa | 1.8 | 1.8 | 3.1† | 4.0 | 4.6 | 5.2 | 9.5‡ | .... | .... | .... | .... | .... |
| Norfolk | 2.1† | 1.4 | 2.4 | 4.6 | 4.1 | 4.3 | 4.1 | 6.7 | 17.0 | .... | .... | .... |
| Atlanta | 3.0† | 0.7† | 4.6† | 5.9† | 7.0 | 13.3 | 10.1 | 12.5 | 14.2 | 11.1 | 10.5 | 8.8 |

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‡ Incomplete data.

bury for three years. Lynn reports no diphtheria or typhoid death during the past five years, New Bedford none for four years. Boston records three diphtheria deaths for 1941, two among residents. Providence reports one death among residents, making only the second such death during the last six years. After a lapse of three years with no death and four years without a death among residents, Lowell records two deaths

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1. Typhoid in the Large Cities of the United States in 1941, J. A. M. A. **119:** 1188 (Aug. 8) 1942.

among residents for 1941. Fall River, reporting three deaths among residents, has recorded one or more deaths each year.

The eighteen cities in the Middle Atlantic states (table 2) continue to hold first place, although now reports ten deaths, all among residents (ten in 1940, twenty-two in 1939). Philadelphia records three deaths, two among residents. There was no death reported in this city in 1940; there were three in 1939. The record for Pittsburgh has reached a new low (one death among residents in 1941; five deaths, four among residents in 1940). Jersey City reports three deaths among residents; Paterson and Erie, one each.

In obtaining data for the cities of the South Atlantic states (table 3), Charlotte (no death in 1941) has been included for the second time. However, for purposes of adequate comparison, the figures for this city have been omitted in calculating rates for the group as a whole. The number of deaths in the nine remaining cities has increased from seventeen in 1940 to twenty-seven in 1941. Of the latter, seventeen were among residents (equal to the total for 1940) and ten among nonresidents. The rate has increased from 0.62 to 0.99 but remains considerably below that of 1939 (1.52). While in 1940 this group of cities stood in third place, 1941 finds the group in sixth place (the East North Central group and the West North Central group having returned to more advanced standings held in 1939 and during the quinquennium 1935-1939). Two cities (Miami, Charlotte) report no death in 1941, and four other cities (Atlanta, Baltimore, Norfolk, Washington) record one third or more of deaths among nonresidents.

TABLE 4.—*Death Rates of Nineteen Cities in East North Central States from Diphtheria (Including Croup) per Hundred Thousand of Population*

| | 1941 | 1940 | 1935-1939 | 1930-1934 | 1925-1929 | 1920-1924 | 1915-1919 | 1910-1914 | 1905-1909 | 1900-1904 | 1895-1899 | 1890-1894 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Grand Rapids | 0.0 | 0.0 | 0.2 | 0.7 | 2.0 | 19.6 | 13.5 | 20.0 | 26.6 | 17.2 | 32.4 | 99.2 |
| Canton | 0.0 | 0.0 | 0.7 | 1.7 | 2.9 | 17.5 | 15.1‡ | .... | .... | .... | .... | .... |
| Youngstown | 0.0 | 0.0 | 0.7 | 3.3 | 10.5 | 18.5 | 11.9 | 40.5 | 33.5 | 28.0 | 17.6 | 28.4‡ |
| South Bend | 0.0 | 0.0 | 1.0 | 1.3 | .... | .... | .... | .... | .... | .... | .... | .... |
| Toledo | 0.0 | 0.0 | 1.1 | 2.7 | 7.2 | 22.4 | 14.1 | 25.4 | 20.4 | 56.8 | 34.6 | 89.3 |
| Akron | 0.0 | 0.0 | 1.8 | 2.7 | 4.9 | 10.4 | 18.9 | 27.8 | 21.8‡ | .... | .... | .... |
| Fort Wayne | 0.0 | 0.0 | 1.9 | 4.0 | 5.1 | 13.1 | 6.3 | .... | .... | .... | .... | .... |
| Dayton | 0.0 | 1.4‡ | 4.3 | 3.6 | 4.6 | 9.4 | 9.3 | 22.1 | 13.3 | 17.3 | 27.4 | 82.9 |
| Columbus | 0.0 | 1.6 | 1.9 | 3.2 | 4.6 | 8.5 | 7.6 | 12.1 | 10.5 | 11.6 | 28.5 | 56.9 |
| Cleveland | 0.2 | 0.1* | 1.0 | 2.5 | 15.3 | 14.7 | 20.0 | 24.6 | 20.8 | 42.6 | 45.3 | 95.7 |
| Milwaukee | 0.2 | 0.3 | 0.4 | 2.1 | 8.5 | 11.4 | 19.3 | 27.8 | 26.4 | 22.7 | 51.7 | 116.2 |
| Detroit | 0.4 | 0.2 | 1.1 | 5.2 | 19.7 | 24.3 | 32.2 | 33.3 | 22.6 | 38.5 | 62.9 | 132.9 |
| Peoria | 0.9 | 0.0 | 3.8 | 5.3 | 4.9 | 7.4 | 10.8 | 10.6 | 10.9‡ | 14.0 | 14.6 | 68.0 |
| Gary | 0.0 | 0.9 | 2.8 | 1.4 | .... | .... | .... | .... | .... | .... | .... | .... |
| Cincinnati | 0.9 | 0.9 | 2.4† | 3.1 | 5.2 | 10.6 | 13.2 | 13.9 | 17.0 | 17.3 | 37.3 | 103.7 |
| Evansville | 1.0 | 1.0 | 1.8 | 3.5 | 3.7 | 13.9 | 14.9 | 16.1 | 21.2 | 13.8 | 18.1 | 69.7 |
| Chicago | 1.0 | 1.1 | 2.2 | 4.5 | 11.7 | 17.5 | 31.2 | 37.9 | 27.0 | 33.9 | 69.7 | 117.3 |
| Flint | 2.0† | 0.0 | 2.8 | 2.7 | 4.5 | 20.9 | 25.5 | 12.7 | 11.0 | 16.8 | 6.9 | 69.2 |
| Indianapolis | 2.1† | 2.6† | 3.6 | 2.9 | 6.6 | 11.7 | 21.4 | 13.5 | 13.3 | 15.9 | 36.4‖ | 97.3‖ |

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‖ Diphtheria deaths from Chapin's Municipal Sanitation.
‡ Incomplete data.

TABLE 5.—*Death Rates of Six Cities in East South Central States from Diphtheria (Including Croup) per Hundred Thousand of Population*

| | 1941 | 1940 | 1935-1939 | 1930-1934 | 1925-1929 | 1920-1924 | 1915-1919 | 1910-1914 | 1905-1909 | 1900-1904 | 1895-1899 | 1890-1894 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Knoxville | 0.0 | 0.9* | 8.2† | 10.0 | 6.3 | 11.2 | .... | .... | .... | .... | .... | .... |
| Nashville | 0.0 | 1.8 | 4.5† | 8.0 | 11.8 | 8.0 | 8.9 | 7.3 | 10.3 | 13.9 | 30.1 | 28.4 |
| Louisville | 0.3* | 0.6 | 2.2 | 6.2 | 4.6 | 10.4 | 9.5 | 9.0 | .... | .... | 39.0‖ | 48.6‖ |
| Memphis | 1.4* | 1.7† | 2.2† | 6.0 | 5.8 | 9.5 | 11.2 | 11.9 | 13.4 | 6.9 | 10.0 | 28.5 |
| Birmingham | 1.5* | 0.7† | 3.1† | 4.4 | 5.4 | 5.3 | 7.2 | 8.3 | 6.2 | 13.4 | 16.5 | 26.3 |
| Chattanooga | 3.9 | 0.8 | 4.0 | 6.8 | 5.9 | 8.7 | 8.9 | .... | .... | .... | .... | .... |

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‖ Diphtheria deaths from Chapin's Municipal Sanitation.
‡ Incomplete data.

hard pressed by the West North Central group. The group rate of 0.17 is slightly lower than that of 1940 (0.20) and less than one half the rate of 1939 (0.37). The new rate represents a new all time low. The West North Central cities are entitled to substantially the same mark of distinction. Twenty-two deaths are recorded in 1941, twenty-six in 1940. Of the former number only three were among nonresidents, in contrast to the relatively high proportion of such deaths in the Southern cities. Ten cities (there were twelve in 1940, nine in 1939) appear in the select list (table 11) with no diphtheria death in 1941 (Buffalo, Camden, Elizabeth, Newark, Reading, Rochester, Scranton, Syracuse, Trenton, Yonkers). Albany reports two deaths both among nonresidents. Rochester records no death for seven years, an impressive accomplishment. Elizabeth reports no death for five years, Yonkers none for four, Trenton none for three years. It is stated that no death from either typhoid or diphtheria has occurred in Yonkers during the last three years, none in Newark for two years, none in Buffalo, Scranton and Trenton during 1941. After seven years without a death, Utica reports one in a resident adult; one death in eight years is a significant record. New York

TABLE 6.—*Death Rates of Nine Cities in West North Central States from Diphtheria (Including Croup) per Hundred Thousand of Population*

| | 1941 | 1940 | 1935-1939 | 1930-1934 | 1925-1929 | 1920-1924 | 1915-1919 | 1910-1914 | 1905-1909 | 1900-1904 | 1895-1899 | 1890-1894 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Duluth | 0.0 | 0.0 | 0.2 | 0.4 | 2.0 | 6.0 | 10.2 | 8.8 | 38.2 | 29.1 | 7.6 | 49.5 |
| Des Moines | 0.0 | 0.0 | 1.5 | 4.3 | 5.2 | 15.1 | 16.6 | 15.1 | 23.8‡ | .... | .... | .... |
| Kansas City, Mo. | 0.0 | 0.0 | 0.9 | 3.3 | 4.7 | 14.4 | 22.8 | 15.7‡ | .... | .... | .... | .... |
| Kansas City, Kan. | 0.0 | 1.6 | 1.6 | 3.5 | 4.6 | 9.8 | 23.1 | 12.4‡ | .... | .... | .... | .... |
| Omaha | 0.0 | 1.8 | 1.4 | 5.1 | 6.4 | 22.9 | 35.8 | 15.8 | 24.5 | 20.5 | 28.2 | 82.9 |
| Minneapolis | 0.2 | 0.6 | 0.6 | 1.7 | 11.9 | 13.4 | 19.9 | 28.3 | 24.4 | 44.6 | 34.0 | 55.0 |
| St. Louis | 0.2 | 1.0 | 2.4† | 4.8 | 10.3 | 16.1 | 24.4 | 23.7 | 19.4 | 43.3 | 62.9 | 67.7 |
| St. Paul | 0.3* | 0.0 | 0.2 | 1.0 | 5.2 | 17.5 | 20.7 | 31.4 | 31.1 | 27.9 | 43.3 | 75.4 |
| Wichita | 0.9 | 0.9 | 1.2 | 5.7 | 4.2 | .... | .... | .... | .... | .... | .... | .... |

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‡ Incomplete data.

TABLE 7.—*Death Rates of Eight Cities in West South Central States from Diphtheria (Including Croup) per Hundred Thousand of Population*

| | 1941 | 1940 | 1935-1939 | 1930-1934 | 1925-1929 | 1920-1924 | 1915-1919 | 1910-1914 | 1905-1909 | 1900-1904 | 1895-1899 | 1890-1894 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Oklahoma City | 0.0 | 0.5 | 2.0 | 5.7 | 10.9 | .... | .... | .... | .... | .... | .... | .... |
| Tulsa | 0.7 | 4.2 | 1.7 | 6.8 | 12.5 | 8.3‡ | .... | .... | .... | .... | .... | .... |
| Houston | 1.0† | 1.0 | 2.6 | 5.6 | 8.2 | 6.4 | 6.1 | 7.8 | 10.5 | 4.2‡ | 2.4 | 1.8 |
| San Antonio | 1.2‡ | 3.6 | 4.1 | 5.7 | 10.3 | 7.7 | 8.7 | 6.7 | 7.6 | 17.1 | 20.6 | 4.4 |
| New Orleans | 1.8‡ | 2.4‡ | 4.3† | 5.5 | 8.5 | 6.5 | 11.6 | 19.6 | 10.2 | 11.5 | 17.1 | 51.3 |
| Fort Worth | 2.2 | 0.6* | 3.9 | 7.2 | 10.8 | 1.7‡ | 2.6‡ | 2.6 | 2.8 | 5.4 | .... | .... |
| Dallas | 2.4 | 2.4‡ | 4.6 | 10.0 | 9.8 | 8.3 | 7.4 | 6.9 | 8.1 | 16.9 | 16.0 | 21.8 |
| El Paso | 6.2† | 1.0 | 4.7 | 8.3 | 7.3 | 20.0 | 17.6 | 29.2 | .... | .... | .... | .... |

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‡ Incomplete data.

Two cities (Atlanta, Norfolk) have rates in excess of 2.0, but of twelve deaths in these cities seven were among nonresidents. Miami is the only city in this group with no death during the past two years. There is no city without a diphtheria and typhoid death in 1941 (table 12). Baltimore reports five deaths, three among residents; Washington, two, one among resi-

dents. Richmond and Tampa each record two deaths among residents (the same as for 1940).

In 1940 Gary was added to the eighteen cities previously included in the East North Central group (table 4). Again the figures for this city have been omitted in the tables for group comparison. The original cities report a slight decrease in the number of deaths from sixty-eight in 1940 to sixty-one in 1941. The rate has decreased from 0.72 to 0.65 (table 16). This group as a whole is in fourth place. Of the sixty-one deaths, only eight were among nonresidents (three in Indianapolis, two each in Detroit and Flint, one in Cincinnati). Chicago reports thirty-four deaths, all among residents (thirty-nine in 1940). Nine cities (there were also nine in 1940) record no death in 1941 (Akron, Canton, Columbus, Dayton, Fort Wayne, Grand Rapids, South Bend, Toledo, Youngstown); Flint and Peoria have been dropped from the honor roll; Columbus and Dayton have been added. Seven cities report no diphtheria deaths in 1940 and 1941 (table 10). Akron, Fort Wayne, Grand Rapids, South Bend and Youngstown record no death during the past four years; Canton and Toledo, none for three years. It is stated that no death from either typhoid or diphtheria has occurred in Fort Wayne and South Bend for four years, none in Canton and Grand Rapids for two years, none in Akron in 1941. Four cities in this group, in addition to the five in table 12, report no typhoid or diphtheria death among residents (Columbus, Dayton, Toledo, Youngstown). Detroit records seven deaths, five among residents (three in 1940, all among residents). Cleveland reports two, both among residents, but the health commissioner doubts the correctness of the diagnosis in one instance. In 1940 Cleveland reported no death among residents, one among nonresidents. Cincinnati (as in 1940) records four deaths, three among residents.

The cities in the East South Central States (table 5) report the same number (fourteen) of deaths in 1941 and 1940, the rate (1.09) being about one third of the five year average (3.37). Only one group, the West South Central, records a higher rate in 1941. Two cities (Knoxville, Nashville) report no death, and three additional cities (Birmingham, Louisville, Memphis) record all deaths among nonresidents. The only city in this group reporting deaths among residents is Chattanooga. This city records five deaths. Nine of the fourteen deaths in the cities of this group were among nonresidents. Birmingham and Memphis each report four deaths among nonresidents. The record of six cities in this group is very impressive. While there is no city in the area with no typhoid and diphtheria death, there are three cities (Knoxville, Memphis, Nashville) in which all such deaths were among nonresidents.

The nine cities in the West North Central states (table 6) report a great decrease in the number of deaths and a rate (0.18) comparable with that of the Middle Atlantic states (0.17). There were only five deaths in this group of cities (eighteen in 1940, eighteen in 1939). The rate compares most favorably with the rate of 1940 (0.66) and the quinquennium 1935-1939 (1.33). There were five cities on the honor roll in 1939, four in 1940 and five in 1941 (Des Moines, Duluth, Kansas City, Kan., Kansas City, Mo., Omaha). St. Paul reports but one death, this among nonresidents (also no death from typhoid). Duluth, Des Moines and Omaha record no diphtheria and typhoid death in 1941; Duluth none during the past three years, Des Moines none for two years. Duluth reports no diphtheria death for six years, Des Moines none for five years, Kansas City, Mo., none for two years (table 10).

Of the five deaths from diphtheria in the group as a whole, four were among residents (two in St. Louis, one each in Minneapolis and Wichita) and one among nonresidents (St. Paul).

The eight cities of the West South Central states (table 7) report a decrease from forty-one deaths in 1940 (forty in 1939) to thirty-four in 1941. The death rate has decreased from 2.00 in 1940 (1.97 in 1939)

TABLE 8.—*Death Rates of Twelve Cities in Mountain and Pacific States from Diphtheria (Including Croup) per Hundred Thousand of Population*

| | 1941 | 1940 | 1935-1939 | 1930-1934 | 1925-1929 | 1920-1924 | 1915-1919 | 1910-1914 | 1905-1909 | 1900-1904 | 1895-1899 | 1890-1894 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Tacoma..... | 0.0 | 0.0 | 0.4* | 3.9 | 9.3 | 12.4 | 7.7‡ | .... | .... | .... | .... | .... |
| Spokane..... | 0.0 | 0.8 | 0.5 | 0.7 | 7.5 | 11.3 | 4.2 | 7.6 | 25.8 | .... | 59.5‖ | 18.1 |
| Oakland..... | 0.3 | 2.0 | 2.5 | 2.0 | 7.4 | 18.8 | 8.1 | 10.3 | 16.1 | 29.1 | .... | .... |
| Seattle..... | 0.5 | 0.5 | 0.4 | 0.4 | 1.4 | 6.6 | 5.5 | 5.2 | 12.5 | 13.4‡ | 27.2‖ | .... |
| Long Beach... | 0.6 | 0.0 | 0.4 | 0.8 | 2.6 | 10.4‡ | .... | .... | .... | .... | .... | .... |
| Los Angeles... | 0.8† | 1.1† | 2.5 | 5.2 | 7.0 | 14.4 | 7.1 | 7.5 | 15.3 | 25.4 | 35.8 | 46.0 |
| San Francisco | 0.9 | 0.9 | 1.6 | 1.2 | 4.6 | 23.0 | 17.0 | 9.2 | 14.4 | 44.2 | 21.6 | 54.8 |
| Portland..... | 1.0† | 1.3 | 0.3 | 1.3 | 6.4 | 11.3 | 6.0 | 12.3 | 12.2 | 30.2 | .... | .... |
| Salt Lake City | 1.3 | 0.0 | 1.0 | 1.3 | 10.1 | 12.5 | 14.5 | 15.1 | 34.2 | 46.0 | 14.8 | 56.7‡ |
| San Diego..... | 2.0 | 1.0† | 2.3 | 2.9 | 6.6 | 12.2 | 10.5 | 8.0 | 5.8 | 2.4 | .... | .... |
| Denver..... | 2.5 | 0.3 | 3.3 | 3.9 | 8.9 | 23.2 | 6.7 | 10.2 | 20.8 | 29.6 | 27.3 | 130.2 |
| Sacramento... | 3.8† | 5.7 | 3.1 | 4.1 | .... | .... | .... | .... | .... | .... | .... | .... |

* All diphtheria deaths were stated to be in nonresidents.
† One third or more of the reported diphtheria deaths were stated to be in nonresidents.
‖ Diphtheria deaths from Chapin's Municipal Sanitation.
‡ Incomplete data.

TABLE 9.—*Three Cities with Highest Diphtheria Rate for 1941*

| | |
|---|---|
| El Paso | 6.2† |
| Chattanooga | 3.9 |
| Sacramento | 3.8† |

† One third or more of the reported diphtheria deaths were stated to be in nonresidents.

TABLE 10.—*Twenty-Seven Cities with No Diphtheria Deaths in 1940 and 1941*

| | | |
|---|---|---|
| Akron † | Grand Rapids † | South Bend † |
| Bridgeport | Kansas City, Mo. | Syracuse |
| Cambridge | Lynn ** | Tacoma |
| Camden | Miami | Toledo †† |
| Canton †† | Newark | Trenton †† |
| Des Moines ** | New Bedford † | Waterbury †† |
| Duluth * | New Haven † | Worcester |
| Elizabeth ** | Rochester ¶ | Yonkers † |
| Fort Wayne † | Somerville †† | Youngstown † |

* No diphtheria death in six years.
** No diphtheria death in five years.
† No diphtheria death in four years.
†† No diphtheria death in three years.
¶ No diphtheria death in seven years.

TABLE 11.—*Forty *Cities with No Diphtheria Deaths in 1941*

| | | |
|---|---|---|
| Akron | Hartford | Rochester |
| Bridgeport | Kansas City, Kan. | Scranton |
| Buffalo | Kansas City, Mo. | Somerville |
| Cambridge | Knoxville | South Bend |
| Camden | Lynn | Spokane |
| Canton | Miami | Syracuse |
| Charlotte | Nashville | Tacoma |
| Columbus | Newark | Toledo |
| Dayton | New Bedford | Trenton |
| Des Moines | New Haven | Waterbury |
| Duluth | Oklahoma City | Worcester |
| Elizabeth | Omaha | Yonkers |
| Fort Wayne | Reading | Youngstown |
| Grand Rapids | | |

* Thirty-nine without Charlotte.

to 1.66 in 1941. Fifty per cent of the deaths in 1941 (seventeen of thirty-four) were among nonresidents. But one city (Oklahoma City) appears on the honor roll. In four cities (Houston, San Antonio, New Orleans, El Paso) it is stated that one third or more of deaths occurred among nonresidents. Three cities report rates in excess of 2.0 (Fort Worth, Dallas, El Paso). Oklahoma City records no diphtheria and typhoid death in 1941 (table 12). Tulsa reports one death among residents (six in 1940). Houston records four deaths, one among residents (four among residents in 1940). San Antonio reports three deaths, one among residents (nine in 1940, seven among residents). New Orleans records nine deaths, three among residents (twelve in 1940, four among residents). El Paso reports six deaths, two among residents (one among residents in 1940). It is stated that, of seven deaths in Dallas, five were among residents (in 1940 of seven deaths four were among residents). Fort Worth reports four deaths, all among residents (in 1940 there was one death among nonresidents).

TABLE 12.—*Twenty Cities with No Diphtheria and Typhoid Deaths in 1941*

| | | |
|---|---|---|
| Akron | Grand Rapids * | Scranton |
| Buffalo | Hartford | Somerville |
| Cambridge * | Lynn †† | South Bend † |
| Canton * | Newark * | Spokane |
| Des Moines * | New Bedford † | Trenton |
| Duluth ‡ | Oklahoma City | Yonkers † |
| Fort Wayne † | Omaha | |

* No diphtheria or typhoid deaths in two years.
‡ No diphtheria or typhoid deaths in three years.
† No diphtheria or typhoid deaths in four years.
†† No diphtheria or typhoid deaths in five years.

TABLE 13.—*Five Cities in Which All Diphtheria Deaths in 1941 Were Stated to Be in Nonresidents*

| | | |
|---|---|---|
| Albany | St. Paul | Louisville |
| Birmingham | Memphis | |

TABLE 14.—*Number of Cities with Various Diphtheria Death Rates*

| | Number of Cities | 40 and Over | 20 and Over | 10 and Over | 5 and Over | Under 5 | 0.0 |
|---|---|---|---|---|---|---|---|
| 1890-1894 | 64 | 52 | 60 | 61 | 62 | 2 | 0 |
| 1895-1899 | 66 | 34 | 53 | 63 | 65 | 1 | 0 |
| 1900-1904 | 68 | 22 | 46 | 64 | 66 | 2 | 0 |
| 1905-1909 | 72 | 3 | 43 | 66 | 71 | 1 | 0 |
| 1910-1914 | 79 | 1 | 36 | 63 | 78 | 1 | 0 |
| 1915-1919 | 84 | 0 | 25 | 62 | 81 | 3 | 0 |
| 1920-1924 | 88 | 0 | 14 | 65 | 86 | 2 | 0 |
| 1925-1929 | 92 | 0 | 1 | 22 | 67 | 25 | 0 |
| 1930-1934 | 93 | 0 | 0 | 0 | 24 | 69 | 0 |
| 1935 | 93 | 0 | 0 | 2 | 17 | 76 | 19 |
| 1936 | 93 | 0 | 0 | 0 | 5 | 69 | 19 |
| 1937 | 93 | 0 | 0 | 0 | 3 | 70 | 20 |
| 1938 | 93 | 0 | 0 | 0 | 3 | 66 | 24 |
| 1939 | 93 | 0 | 0 | 0 | 2 | 59 | 32 |
| *1940 | 93 | 0 | 0 | 0 | 0 | 53 | 40 |
| *1941 | 93 | 0 | 0 | 0 | 1 | 53 | 39 |

* Charlotte, Gary and Sacramento omitted.

In 1940 Sacramento was added to the eleven cities included in the Mountain and Pacific group (table 8). The figures for this city have been omitted in the tables for group comparison. The original cities report the same number of deaths as in 1940 (thirty-nine). This group of cities stands in fifth place, with a rate of 0.93. There are two cities on the honor roll (Spokane, Tacoma). Tacoma has continued on the honor list for two years. Long Beach, which previously reported no death in six years, records one death among residents. Salt Lake City, with no death in 1940, reports two among residents in 1941. Of the thirty-nine deaths in the group as a whole, twelve were among nonresidents. Spokane is the only city in the group that reports no diphtheria and typhoid death in 1941. Two cities (Denver, Sacramento) record a rate in excess of 2.0. Denver reports eight deaths, six among residents; Sacramento records four, two among residents. It is stated that, of twelve deaths in Los Angeles, eight were among nonresidents (of seventeen in 1940, eight were among nonresidents). San Francisco reports six deaths, all

TABLE 15.—*Total Diphtheria Death Rates for Eighty-Eight Cities, 1923-1941* *

| | Population | Diphtheria Deaths | Diphtheria Death Rate per 100,000 of Population |
|---|---|---|---|
| 1923 | 31,060,848 | 4,078† | 13.13 |
| 1924 | 31,722,841 | 3,439 | 10.84 |
| 1925 | 32,384,834 | 3,133 | 9.67 |
| 1926 | 33,046,827 | 3,106 | 9.40 |
| 1927 | 33,708,820 | 3,493 | 10.36 |
| 1928 | 34,370,813 | 3,176 | 9.24 |
| 1929 | 35,032,806 | 2,738 | 7.82 |
| 1930 | 35,719,180 | 1,827 | 5.22 |
| 1931 | 35,821,890 | 1,366 | 3.81 |
| 1932 | 35,916,317 | 1,191 | 3.32 |
| 1933 | 36,032,205 | 861 | 2.38 |
| 1934 | 36,166,434 | 821 | 2.27 |
| 1935 | 36,348,921 | 771 | 2.12‡ |
| 1936 | 36,549,325 | 551 | 1.51‡ |
| 1937 | 36,751,422 | 571 | 1.55# |
| 1938 | 36,956,409 | 467 | 1.26¶ |
| 1939 | 37,160,779 | 326 | 0.88° |
| 1940 | 37,309,215 | 225 | 0.60‖ |
| 1941 | 37,309,215†† | 209 | 0.56** |

* The five following cities are omitted from this summary, because data for the full period are not available: Jacksonville, Miami, Oklahoma City, South Bend and Utica.
† Data for Fort Worth lacking.
‡ The rate for the ninety-three cities in 1935 is 2.13 (population 37,025,179, diphtheria deaths 789). The corresponding rate for 1936 is 1.52 (population 37,241,414, diphtheria deaths 567).
# Rate for ninety-three cities in 1937 was 1.55 (population 37,459,339, diphtheria deaths 583).
¶ Rate for ninety-three cities in 1938 was 1.26 (population 37,680,155, diphtheria deaths 477).
° Rate for ninety-three cities in 1939 was 0.87 (population 37,900,854, diphtheria deaths 330).
‖ Rate for ninety-three cities in 1940 was 0.60 (population 38,060,602, diphtheria deaths 229).
** Rate for ninety-three cities in 1941 was 0.56 (population 38,060,602, diphtheria deaths 213).
†† 1940 census figures used.

TABLE 16.—*Total Diphtheria Death Rates per Hundred Thousand of Population for Ninety-Three Cities According to Geographic Divisions*

| | Diphtheria Deaths | | Diphtheria Death Rates | | | | |
|---|---|---|---|---|---|---|---|
| | Population * | 1941 | 1940 | 1941 | 1940 | 1935-1939 | 1930-1934 | 1925-1929 |
| New England | 9,579,152 | 11 | 6 | 0.43 | 0.23 | 0.85 | 3.38 | 8.34 |
| Middle Atlantic | 13,129,185 | 22 | 26 | 0.17 | 0.20 | 0.65 | 2.50 | 9.97 |
| South Atlantic | 2,727,985 | 27 | 17 | 0.99 | 0.62 | 2.18 | 3.54 | 7.37‖ |
| East North Central | 9,386,378 | 61 | 68 | 0.65 | 0.72 | 1.82 | 3.66 | 11.21† |
| East South Central | 1,286,747 | 14 | 14 | 1.09 | 1.09 | 3.37 | 6.36 | 6.34 |
| West North Central | 2,716,484 | 5 | 18 | 0.18 | 0.66 | 1.33 | 3.22 | 7.82 |
| West South Central | 2,048,692 | 34 | 41 | 1.66 | 2.00 | 3.85 | 6.55 | 9.24‡ |
| Mountain and Pacific | 4,186,039 | 39 | 39 | 0.93 | 0.93 | 1.71 | 2.69 | 6.28 |

‖ Lacks data for 1925 for Jacksonville and Miami.
† Lacks data for South Bend.
‡ Lacks data for Oklahoma City for 1925 and 1926.
* 1940 Census figures used.

among residents (six in 1940, four among residents). The health director states that all six fatalities in 1941 were of persons over 25 years of age. Oakland records one death and Seattle two, all among residents; Portland reports three deaths, two among residents; San Diego records four deaths, three among residents.

Of the entire ninety-three cities there was one (none in 1940) with a rate of 5.0 and over (table 14). In this city (El Paso) of six deaths four were among nonresidents. The number of cities with no deaths from diphtheria has decreased by one (forty to thirty-nine). The number of cities with rates below 5.0 has remained at fifty-three. For the eighty-eight cities (table 15) for which data are available since 1923 there occurred two hundred and nine deaths from diphtheria in 1941, significantly lower than for previous years (two hundred and twenty-five in 1940, three hundred and twenty-six in 1939). The rate for this group of cities is for the third consecutive year less than 1.0. The rate for the ninety-three cities is the same as that for the eighty-eight cities (0.56) and establishes a new low record. The actual number has decreased by sixteen (from two hundred and twenty-nine to two hundred and thirteen). This decrease is far less impressive than that of one hundred and one for the preceding interval (three hundred and thirty in 1939, two hundred and twenty-nine in 1940).

The health officers did not report any extensive outbreaks of diphtheria. There is evidence of a tendency for this disease to become relatively more prevalent among the higher age groups as the protective programs for infants, preschool and school children continue.

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## *Council on Pharmacy and Chemistry*

### REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

AUSTIN E. SMITH, M.D., Acting Secretary.

### AMINOACETIC ACID AND ACCEPTED BRANDS OMITTED FROM N. N. R.

Aminoacetic acid was first included in New and Nonofficial Remedies in 1936. The following brands have been accepted: Aminoacetic Acid-Calco, Aminoacetic Acid-Mallinckrodt, Aminoacetic Acid-Merck, Aminoacetic Acid-Paul Lewis, Aminoacetic Acid-Pfanstiehl. In considering the reacceptance of one of these brands at the time its acceptance period expired, it was suggested that the use of this agent for the conditions stated in New and Nonofficial Remedies be investigated. In order to implement this suggestion the following letter was sent to a selected list of twelve neurologists:

"Aminoacetic acid has been accepted since 1935 for inclusion in New and Nonofficial Remedies and described as outlined in the enclosed tear sheets.

"The Council members have voted to reconsider this product and suggested that the Secretary get in touch with outstanding neurologists. Accordingly, we are taking the liberty of asking if you would care to make any comments on the present status of aminoacetic acid in your respective field. These comments will be presented to the Council members to help them in their reconsideration of whether or not aminoacetic acid should be retained in New and Nonofficial Remedies.

"It is hoped that this request does not prove too great an imposition on your time."

Of this list nine replies were received. For the sake of record the replies are reproduced without the names of the consultants.

*First Consultant:*

I have given up its use entirely. I have given the drug a good trial in myasthenia gravis, progressive muscular atrophy, amyotrophic lateral sclerosis and in various forms and stages of muscular dystrophy without observing any lasting benefits.

*Second Consultant:*

I used a great deal of it some years ago in cases of myasthenia gravis and muscular atrophy without any appreciable effect. I have not used it for several years and probably never shall.

*Third Consultant:*

I have had very little experience with this compound. I have used it in progressive muscular dystrophy but have never seen anything I thought very advantageous from its use. Recently I have not made use of it at all.

*Fourth Consultant:*

I have seen no clinical improvement from its use.

*Fifth Consultant:*

I used it extensively for a selected group of patients with progressive muscular dystrophy for over a year. Results were uniformly disappointing with no evidence of improvement in any of the patients. I feel it has no place in the treatment of muscular or neural disorders.

*Sixth Consultant:*

My experience has been that this substance is of no practical value in the treatment of the muscular atrophies or dystrophies. My experience is somewhat limited and must be judged on this basis.

*Seventh Consultant:*

In 1939 H. R. Viets and R. S. Schwab (The Diagnosis and Treatment of Myasthenia Gravis, THE JOURNAL, Aug. 12, 1939, p. 559) wrote as follows: "Aminoacetic acid, contrary to our expectations from Boothby's reports, proved to be of no value in 17 cases. As much as 45 Gm. a day in divided doses, a larger amount than Boothby recommended, was given." This consultant is aware that, with the additional experience of two years, these men would not care to change the statement except to add more cases.

*Eighth Consultant:*

It has seemed to me that its use in large doses helped to delay progressive atrophy. I have no proof; this is only a clinical impression gained from 5 or 6 cases.

*Ninth Consultant:*

I have not been using aminoacetic acid in recent years and my earlier experience was limited to a few cases of asthenia of doubtful type. In those instances the creatine excretion was diminished under glycine administration, but the experiments were not conclusive because other measures such as psychotherapy were also employed, and I have seen more striking improvement in comparable cases without glycine.

In "Biochemistry of Disease" the Bodanskys reviewed the literature on this subject. They state ". . . Glycine has been recommended as a therapeutic agent in progressive muscular dystrophy by a considerable number of clinicians. The reports concerning its therapeutic value are, however, very conflicting. A few have described definite improvement, but the majority of reports deny that amino acid is of any definite value. . . ."

After consideration of the comments of the neurologists consulted, a letter of inquiry was sent to the manufacturers of accepted brands of aminoacetic acid asking that they forward any available evidence to warrant continued inclusion of this agent in New and Nonofficial Remedies. From the replies received from these firms there is no indication of evidence for the usefulness of this drug that would justify its retention.

In view of the foregoing the Council voted to omit Aminoacetic Acid and the accepted brands from New and Nonofficial Remedies.

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SATURDAY, AUGUST 29, 1942

## NEWER KNOWLEDGE OF THE MECHANISM OF TUBERCULOSIS IMMUNITY

The exceedingly ingenious tissue transplantation technics reported by Lurie and Zappasodi [1] of the Henry Phipps Institute, University of Pennsylvania, have added materially to current knowledge of the intracellular or nonhumoral factors in acquired immunity to tuberculosis. Early failures to produce an effective antituberculosis serum led to the conclusion that acquired immunity to this disease is a much more complex process than the simple antitoxic immunity against diphtheria infection. An elaborate theory of "partial antibodies" was formulated by Deycke and Much [2] to explain this complexity. According to this theory, acquired antituberculosis immunity is due to the formation of four distinct groups of partial antibodies. Three of these are assumed to exist in the blood stream, while the fourth is found only in the cytoplasms of fixed tissue cells. This theory was partially confirmed by American investigators,[3] who found that the acquired power of prompt intraperitoneal lysis of the tubercle bacillus cannot be transferred serologically even by repeated massive blood transfusions from tuberculoimmune donors. Isolated peritoneal tissues from these immune donors were found to have the power of lysing tubercle bacilli in vitro. Lysis did not occur in control tests with normal peritoneal tissues even when suspended in tuberculoimmune serum.

The essential bacteriostatic factor in immune fixed tissue cells has been studied in greater detail by Lurie [4] and his collaborators of the University of Pennsylvania. They have shown that the dominant defensive cells in acquired immunity to tuberculins are the mononuclear phagocytes. These show heightened physiologic activities in tuberculous animals, expressed by an increased rate of cell division and by increased phagocytosis of india ink, pyogenic cocci and other particulate matter. Not only are tubercle bacilli taken up more rapidly in immune macrophages but the ingested bacilli fail to multiply within the body of the phagocytes, abundant intracellular proliferation taking place in control tests with nonimmune macrophages.

Numerous unsuccessful attempts have been made to determine the mechanism of this intracellular growth inhibition by in vitro studies of leukocytes [5] and fixed tissue cells.[6] These have usually given inconclusive results, owing to the difficulty of maintaining such cells at full physiologic vigor for sufficient periods of time outside the animal body. To avoid this difficulty Lurie attempted the same analysis by tissue transplantation methods, the anterior chamber of the eye being the selected transplantation site. The anterior chamber of the eye serves as an almost perfect medium [7] for the cultivation of homologous normal and pathologic tissue cells.

Normal and immunized rabbits were given subcutaneous injections of human or bovine tubercle bacilli suspended in salt solution containing india ink. The regional lymph nodes were removed two days later. These glands were cut into fine particles and repeatedly washed in Tyrode solution, and several particles were introduced into the anterior chamber of the eye of an albino rabbit. Immune tissue fragments were introduced into one eye, and control nonimmune fragments in the opposite eye of the same animal. Samples of the same tissues were used for control bacteriologic and microscopic study. Similar implantations were made with immune and nonimmune bone marrows from rabbits injected intravenously two days previously with tubercle-carbon suspensions.

Growth of the implants was observed for ten to fourteen days. At the end of this time the rabbits were killed and the implanted cells studied both microscopically and by quantitative culture methods. In a typical experiment the number of colonies cultured from 100 mg. of implanted normal cells was forty times the number of bacilli originally present in these cells. In parallel tests with immune tissues there was only a fourfold increase in bacterial count. In all cases the cells of immune rabbits that had ingested tubercle bacilli in vivo and had grown in the anterior chamber of normal rabbits had greatly inhibited the normal multiplication of ingested tubercle bacilli.

This technic, of course, did not rule out the possible bacteriostatic role of humoral antibodies adherent to the injected bacteria. Implantations into the anterior chambers of normal rabbits were therefore made of

1. Lurie, M. B.: J. Exper. Med. **75**: 247 (March) 1942.
2. Deycke, K., and Much, H.: München. med. Wchnschr. **40**: 119, 190, 1913.
3. Manwaring, W. H., and Bronfenbrenner, Joseph: J. Exper. Med. **18**: 610, 1913.
4. Lurie, M. B.: J. Exper. Med. **69**: 579 (April) 1939.
5. Hanks, J. H., and Bruckenbrough, E.: Am. Rev. Tuberc. **41**: 605, 1940.
6. Rich, A. R., and McCurdock, H. A.: Bull. Johns Hopkins Hosp. **44**: 273, 1929.
7. Greene, H. S. N., and Saxton, J. A., Jr.: J. Exper. Med. **67**: 691 (March) 1938. Lucké, Baldwin, and Schlumberger, H. G., ibid. **72**: 321 (Sept.) 1940.

washed (serum free) normal and immune macrophages that had taken up tubercle bacilli in vitro. These cells were obtained from normal or immune rabbits which had received intrapleural injections of acacia solution four or five days previously.[8] The experiments showed that there is no appreciable increase in phagocytosis by normal macrophages when the ingestion occurs in the presence of immune serum, compared with control tests in normal serum. There was also no acquired power of bacteriostasis as a result of such exposure to immune serum. Cells obtained from immunized animals and washed free from immune body fluids were more actively phagocytes in the presence of normal serum and inhibited subsequent intracellular proliferation of the ingested bacilli ten times more effectively than did normal macrophages similarly tested.

From a multiplicity of data of this type Lurie concludes that active tuberculosis confers increased bacteriostatic properties for ingested tubercle bacilli on fixed tissue phagocytes and that this acquired immunity is independent of circulating antibodies. Demonstration of this fixed tissue bacteriostaticity has clinical interest in numerous other infectious diseases, particularly virus infections, in which available evidence suggests the relative unimportance of so-called circulating antibodies. Whether or not the intracellular bacteriostat can be extracted from tuberculoimmune macrophages has not yet been determined.

## FEEBLEMINDEDNESS AND HEREDITY

The story of a feebleminded family given the pseudonym "Kallikak" was published in 1912 by Goddard. Sociologists, psychologists and geneticists varied widely in their acceptance of his conclusions. In 1925 Dr. Abraham Myerson in a book entitled "The Inheritance of Mental Disease" took sharp issue with Goddard's conclusions. This was appropriate and fortunate for the science of human genetics. Unfortunately the book also contained some misstatements regarding Goddard's study. Others have misinterpreted some of his conclusions.

Like all authors, Professor Goddard objects to being misquoted and misinterpreted. In his recent article in *Science* he[1] points out some of the misquotations and some of the misinterpretations which have appeared in the literature. Two questions which naturally arise in connection with this reopening of a discussion of the Kallikak study are By what criteria should this study be judged? and How closely do the conclusions which are drawn by the author agree with present opinion? These are not easy questions to answer because the whole subject concerned is still in a controversial state.

In terms of present day requirements for an analysis of the relative roles of heredity and environment in the determination of the variability observed in a mental character, the Kallikak study falls far short in rigor and in analytic technic. It makes use neither of refined psychologic tests nor of detailed statistical methods. However, it must be viewed in the light of the psychologic and genetic knowledge of 1914. When thus considered, it compares favorably with studies in other sciences at similar stages of development.

As regards the agreement between the conclusions drawn by Goddard in his book published in 1914 and present opinion, there is nothing definite which can be said. However, a few comparisons can be made. In chapter VIII of "Feeblemindedness: Its Causes and Consequences," Goddard leaves the impression that he considers intelligence a unitary character. This point of view is certainly indefensible today, and probably Professor Goddard would not even want to defend this thesis now. Feeblemindedness is not even considered a unit character by modern investigators. Many types and degrees of it are recognized. In the same chapter the author argues for the inheritance of feeblemindedness as a simple recessive. This conclusion may not be far from the truth for certain types of feeblemindedness. There exists at least considerable evidence that certain types are inherited in a relatively simple fashion and that some of the responsible genes behave as recessives. Other types give evidence of being due to genes inherited as dominants.

In summarizing present opinion regarding the relative roles of heredity and environment in the determination of feeblemindedness, the following statements seem pertinent: 1. Feeblemindedness is a general name for low mentality and is not a unitary character. There are many types and degrees of it. 2. Some types of feeblemindedness are the result of variations in the environment: birth injury, lack of iodine, infectious diseases, unfavorable cultural conditions, and the like. 3. Some types of feeblemindedness are the result of variations in hereditary factors. Whether a variation in a single genetic locus may be responsible for feeblemindedness is as yet uncertain, but certain types appear to involve variations in only one or at least in only a limited number of loci. 4. Some types may be the result of a combination of unfavorable environmental and hereditary factors. 5. Of the hereditary types of feeblemindedness which have been reported, some give evidence of being due to a single recessive gene or to a limited number of recessive genes. A few appear to be inherited in a dominant fashion. A few studies suggest a role played by sex linked genes. 6. Improvement in the performance of all feebleminded individuals may be expected by improving environmental conditions. However, at least for the types which have a

8. Robertson, O. H., and Van Sant, Helen: J. Immunol. **37**: 571 (Dec.) 1939.

1. Goddard, Henry H.: In Defense of the Kallikak Study, Science **95**: 574 (June 5) 1942.

hereditary basis, there appears to be a definite limitation of the extent to which improvement may be expected.

Whatever the final conclusions concerning the merits of the original Kallikak study, it can be recognized that Goddard gave an enormous stimulus to scientific investigation of inheritance of feeblemindedness and indeed to the entire science of human genetics.

## Current Comment

### REPORTS OF THE COUNCIL ON PHARMACY AND CHEMISTRY

The Council on Pharmacy and Chemistry recently issued the thirty-third edition of the Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association.[1] This volume contains in compact form not only the reports of the Council which have been published in THE JOURNAL during the past year but also some additional reports which were not considered of sufficient importance to be published in THE JOURNAL. The reports may be divided into four classes: reports rejecting products as not being acceptable for inclusion in New and Nonofficial Remedies, reports omitting from New and Nonofficial Remedies products that have previously been accepted, reports on the nomenclature of various substances and reports in which the Council gives decisions of general interest or summarizes the latest scientific knowledge concerning certain topics. The last classification includes the largest number of reports. One article deals with the developments in bacteriophage therapy since the previous report of the Council in 1934. Other reports bring to the present day the status of such products as aluminum hydroxide preparations, antipneumococcic serums, cyclopropane, human blood plasma and serum, human convalescent poliomyelitis serum, human convalescent mumps serum and sulfadiazine. Such topics as ion transfer (iontophoresis), halogenated vegetable oils for bronchography and the problem of lipid pneumonia and the sympathomimetic amines as epinephrine substitutes are discussed. The nomenclature reports deal for the most part with the Council's adoption of nonproprietary designations for comparatively new products such as diethylstilbestrol, menadione and sulfadiazine. Explanations are given for the omission at this time of products which have previously been included in New and Nonofficial Remedies. In most cases the N. N. R. description is included in the report as a matter of record. The volume also includes the reports rejecting various products—which have either been submitted by the manufacturer or considered on the Council's own initiative—and which have been found not acceptable for inclusion in New and Nonofficial Remedies. Also incorporated is a brief summary of the decisions arrived at by the Council at its latest meeting.

1. Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1941, with the Comments That Have Appeared in THE JOURNAL, Chicago, American Medical Association, 1942, price $1.

### RESEARCH IN CANCER AT THE MEMORIAL HOSPITAL

The Biennial Report of the Memorial Hospital for the Treatment of Cancer and Allied Diseases in New York, just available,[1] indicates the contribution which this institution is making in research. Investigations have been carried forward by means of animal experiments, chemical studies, examinations of the role of diet in cancer, by study of cancer in man, search for cancer producing substances, by attempts to starve the cancer cells and in problems of leukemia and the vitamins. An additional group of studies is in progress in an attempt to short-circuit the more prolonged investigations and to develop a method of cure without a knowledge of the mechanisms by which the cure would be effected. This is a purely empiric study, involving experiments which so far have employed some seventy different compounds for their effect in killing cancer cells. The results already secured may have far reaching significance. The chemicals which appear to have an anticancer effect are characterized by a common structure. They prove apparently that there is a real difference between cancer cells and normal cells in their sensitivity to certain types of chemicals.

### INSTITUTES ON WARTIME INDUSTRIAL HEALTH

California has become one of our foremost industrial states. Inevitably physicians will be required to meet vastly expanded demands for industrial health service. A series of wartime industrial health institutes is now being offered in such strategically located industrial areas as San Francisco, Crockett, Oakland, San Diego, Inglewood, Glendale and Huntington Park. These meetings have been developed by the California State Department of Health in cooperation with the California Medical Association and the Western Association of Industrial Physicians and Surgeons. The programs are designed to present concisely and practically the important clinical, administrative and socioeconomic problems which a physician is likely to encounter in his first engagements with industry and to dramatize as well the agencies for consultation and assistance which are already at his command. Naturally the concept of health in relation to expanded wartime production is featured. Outside of military service the most important contribution that a physician can make to the war effort lies in the direction of industrial health. This current educational activity in California and in a few other states is substantial recognition that something beyond simple acknowledgment of the importance of improved physical welfare of workers is necessary. These institutes on industrial health are highly desirable as introductory instruction both to physicians and to industrialists. They should be followed by suitable provision for more extended postgraduate study using resources of medical schools, industrial hygiene laboratories, well conducted industrial medical services and other agencies under stimulation and leadership of active committees on industrial health in state and county medical societies.

1. Record of Service, Biennium Report, 1940-1941, Memorial Hospital for the Treatment of Cancer and Allied Diseases.

# MEDICINE AND THE WAR

***In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war, and such other information and announcements as will be useful to the medical profession.***

## CONFERENCE ON VENEREAL DISEASE CONTROL IN WARTIME

Venereal disease and the war effort will be discussed at a conference in Hot Springs National Park, Ark., October 21-24, held under the auspices of the United States Public Health Service in conjunction with the eighth annual meeting of the American Neisserian Medical Society. Surg. Gen. Thomas Parran will preside. State and local health officers, venereal disease control officers, practicing physicians and all others engaged in venereal disease control activities are urged to attend. The governmental, professional and health organizations to be represented at the conference will include the War Department, the Navy Department, the Office of Defense Health and Welfare Services, the American Medical Association, the American Neisserian Medical Society, the American Social Hygiene Association, state and local health departments, and the United States Public Health Service. A tentative program of the conference follows:

### OCTOBER 22, 10 A. M.

#### VENEREAL DISEASE CONTROL MEASURES INFLUENCING THE WAR EFFORT

1. Rehabilitation of Selectees with Syphilis and Gonorrhea. Lieut. Col. Richard H. Eanes, Assistant Director, Medical Division, Selective Service System.
2. Present Venereal Disease and Prostitution Problems as They Relate to the Army. Lieut. Col. T. B. Turner, Director, Venereal Disease Control Division, Preventive Medicine Service, United States Army.
3. Present Venereal Disease and Prostitution Problems as They Relate to the Navy. Capt. C. S. Stephenson, in Charge, Division of Preventive Medicine, Bureau of Medicine and Surgery, United States Navy.
4. The Contribution to the War Effort of the Subcommittee on Venereal Diseases, National Research Council. Dr. J. E. Moore, Baltimore.
5. Private Physician Support of the Wartime Venereal Disease Control Program.

### OCTOBER 22, 2 P. M.

#### THE EPIDEMIOLOGY OF SYPHILIS AND GONORRHEA, 1942

1. The Epidemiology of Gonorrhea as a Stimulus to Prostitution Repression. Dr. Donald H. Williams, Medical Director, Division of Venereal Disease Control, Provincial Board of Health, Vancouver, B. C.
2. Improvement of Present Methods for Extrafamilial Contact Tracing. Miss Mary A. Burke, Consultant in Social Hygiene Nursing, Detroit Department of Health.
3. Difficulties in Case Holding of Selectees Infected with Syphilis. Dr. G. Foard McGinnes, Director, Division of Venereal Disease Control, Tennessee State Department of Health.
4. Defects in the Present Follow-Up Program. Lida J. Usilton, Principal Statistician, Division of Venereal Diseases, U. S. Public Health Service.
5. The Male Investigator in Venereal Disease Control Follow-Up. Dr. Malcolm H. Merrill, Chief, Bureau of Venereal Diseases, California Department of Public Health.

### OCTOBER 23, 9:30 A. M.

#### EIGHTH ANNUAL MEETING, AMERICAN NEISSERIAN MEDICAL SOCIETY

1. The Control of Venereal Disease Among Industrial Workers. Surg. Otis L. Anderson, Assistant Chief, Division of Venereal Diseases, U. S. Public Health Service.
2. Organization and Management of Clinics in a State Gonorrhea Control Program. Dr. F. W. Caudill and Dr. R. E. Teague, Kentucky State Department of Health.
3. Gonococcus Culture Methods. Dr. Charles M. Carpenter, School of Medicine, University of Rochester.
4. Management of Gonorrhea in the Male. Dr. P. S. Pelouze, University of Pennsylvania, Philadelphia.
5. Management of Gonorrhea in the Female. Dr. Robert M. Lewis, Yale University School of Medicine.
6. Hyperpyrexia in Chemoresistant Gonorrhea. Dr. Stafford L. Warren, School of Medicine, University of Rochester.

General discussion led by Dr. Nels A. Nelson, Director, Division of Venereal Disease Control, Maryland Department of Health, and Dr. Adolph Jacoby, New York City Health Department.

### OCTOBER 23, 2 P. M.

#### EIGHTH ANNUAL MEETING, AMERICAN NEISSERIAN MEDICAL SOCIETY

1. Gonococcus Cultures as a Public Health Service: A Preliminary Report. Capt. Daniel Bergsma, Venereal Disease Control Officer, Headquarters, First Army, Governors Island, N. Y.
2. President's Address. Asst. Surg. Gen. R. A. Vonderlehr, Division of Venereal Diseases, U. S. Public Health Service.
3. Gonorrhea from the Standpoint of the Army. Capt. Ernest B. Howard, Venereal Disease Control Officer, Fourth Army Corps Area, Atlanta, Ga.
4. Gonorrhea from the Standpoint of the Navy. Capt. C. S. Stephenson, Division of Preventive Medicine, Bureau of Medicine and Surgery, United States Navy.
5. Résumé of the Year's Research in Gonorrhea. Dr. Alfred Cohn, Department of Health, New York City.
6. Role of Organized Medicine in the Control of Gonorrhea. Dr. Robert S. Breakey, Lansing, Mich.

### OCTOBER 23, 2 P. M.

Demonstration: Technics of Modern Serodiagnostic Tests for Syphilis.

### OCTOBER 24, 9:30 A. M.

#### WARTIME VENEREAL DISEASE CONTROL EDUCATION PROGRAM

1. Relationship Between the Programs of Venereal Disease Control Education and the Repression of Prostitution:
   (*a*) From the point of view of public health. Dr. George M. Leiby, Director, Division of Preventive Medicine, Louisiana State Department of Health.
   (*b*) From the point of view of social protection. Mr. Charles P. Taft, Assistant Director, Office of Defense Health and Welfare Services.
   (*c*) From the point of view of the public. Mr. Capus Waynick, Director, Demonstration of Public Health Education Measures in the Control of Venereal Diseases, Raleigh, N. C.
2. Venereal Disease Control Education Program in the Armed Forces:
   (*a*) Army. Major William A. Brumfield, Venereal Disease Control Division, Preventive Medicine Service, U. S. Army.
   (*b*) Navy. Capt. C. S. Stephenson, U. S. Navy.
3. Current Status of Venereal Disease Education. Surg. Gen. Thomas Parran, U. S. Public Health Service.

### OCTOBER 24, 2 P. M.

#### RESEARCH INFLUENCING THE WARTIME VENEREAL DISEASE CONTROL PROGRAM

1. Progress in Investigations of the Intensive Therapy of Syphilis. P. A. Surgeon Harry Eagle, U. S. Public Health Service Syphilis Research Center, Baltimore.
2. New Serologic Tests for Syphilis and Their Demonstrated Efficiency. Dr. Arthur H. Sanford, Mayo Clinic, Rochester, Minn.
3. Progress in the Wartime Management of Gonorrhea. Dr. P. S. Pelouze, University of Pennsylvania, Philadelphia.
4. Relationship Between Venereal Disease Control and the Joint Army and Navy Committee on Welfare and Recreation. Brig. Gen. F. H. Osborn, Chief of Special Service, United States Army.
5. Problems Involved in the Adaptation of Recent Scientific Discoveries to the Wartime Control of the Venereal Diseases. Dr. John H. Stokes, University of Pennsylvania, Philadelphia.

OCTOBER 21, 2 P. M.

TECHNICS OF VENEREAL DISEASE EDUCATION

1. Introductory comments. Asst. Surg. Gen. R. A. Vonderlehr, U. S. Public Health Service.
2. Presentation of a Typical Venereal Disease Education Problem for Discussion by Panel and Conference:

Discussion Leaders:

State Health Officer: Dr. Felix J. Underwood, Executive Officer, State Board of Health, Jackson, Miss.

State Venereal Disease Control Officer: Dr. Malcolm H. Merrill, Chief, Bureau of Venereal Diseases, Department of Health, San Francisco.

Local Health Officer: Dr. Hugh Leavell, City Health Officer, Louisville, Ky.

Local Venereal Disease Control Officer: Dr. L. W. Shaffer, Director, Social Hygiene Division, Department of Health, Detroit.

Community Resources: Dr. Lucy Morgan, Health Education Consultant, P. H. S., Community Organization for Health Education, Fayetteville, N. C.

Voluntary Health Agency: Dr. William F. Snow, Director, American Social Hygiene Association.

Health Department Public Relations: Miss Ann Wilson Haynes, Public Information Editor, Department of Public Health, San Francisco.

Clinic Management: Dr. Nels A. Nelson, Director, Division of Venereal Disease Control, State Department of Health, Baltimore.

Gonorrhea: Dr. Charles M. Carpenter, School of Medicine, University of Rochester.

Syphilis Case Control: Miss Anne Sweeney, Vanderbilt University Hospital, Nashville, Tenn.

Gonorrhea Case Control: Mr. Morris S. Wortman, University of Missouri, Columbia, Mo.

Social Protection: Mr. Arthur E. Fink, Regional Supervisor, Division of Social Protection, Birmingham, Ala.

Work Projects Administration: Mr. T. Lefoy Richman, Informational Specialist, U. S. Public Health Service.

Nursing: Miss Donna Pearce, Public Health Nursing Consultant, U. S. Public Health Service.

General Health Education: Miss Elizabeth Bohnenberger, Director of Health Education, State Board of Health, Jacksonville, Fla.

## RESTRICT SALE OF ALL QUININE

The Health Supplies Branch of the War Production Board called attention, August 17, to the fact that all stocks of quinine and totaquine, no matter how small, have been subject to the restrictions of Conservation Order M-131 since June 19.

Prior to that date, stocks of 50 ounces or less could be freely sold. Since June 19, retail druggists and all other sellers have not been permitted to sell quinine or totaquine for any purpose except as an antimalarial agent. The order extends to powder, capsules, solutions, pills and tablets and to quinine or totaquine stocks of all other descriptions whether or not packages have been opened.

The same sales restrictions apply to cinchonine, cinchonidine and quinidine, which are covered by Order M-131-a. No stocks of these may be sold except as an antimalarial agent and, in the case of quinidine, for the treatment of cardiac disorders.

The branch stresses that these drugs are urgently needed for military antimalarial use. Supplies are limited since their raw material source, cinchona bark, comes in most part from Java.

Druggists and pharmaceutic and proprietary manufacturers may not use their stocks of quinine or other alkaloids of cinchona bark in the manufacture of products which are designed for other than permitted purposes. These restrictions extend as well to dispensing of the drugs on physicians' prescriptions.

The practical effect of these regulations as far as manufacturers are concerned is to prohibit the use of their stocks in the manufacture of products such as elixir of iron, quinine and strychnine phosphates, coryza tablets and other formulas designed for treatment of other than malarial ailments. However, any such products which were manufactured prior to the effective date of the order controlling the particular drug involved may be sold without restriction.

Druggists having stocks of quinine, cinchonine, cinchonidine and quinidine in excess of their requirements for the permitted uses are urged to return the drugs to their source of supply.

## OPINION ON USE OF CINCHONA AND CINCHONA ALKALOIDS FOR THE TREATMENT OF MALARIA

The following notice is from the Food and Drug Administration, Washington, D. C.:

As a guide to its activities under the provisions of the Federal Food, Drug and Cosmetic Act in the consideration of preparations offered for the treatment of malaria, the Food and Drug Administration requested an expression of opinion from the National Research Council as to the use of the cinchona alkaloids in this field. The request was referred by the Council to its Division of Medical Sciences, Subcommittee on Tropical Diseases. We are now in receipt of a report from the National Research Council in which it states that a preparation of one or more of the crystallizable cinchona alkaloids (quinine, quinidine, cinchonine, cinchonidine) for the treatment of malaria should provide daily for seven consecutive days, for adults, at least 20 grains of the alkaloid or alkaloids.

The minimum amounts of these alkaloids which should be provided daily for the same period for children are as follows:

| Age | Grains | Age | Grains |
|---|---|---|---|
| Under 1 year | 2½ | 7 to 8 years | 12½ |
| 1 to 2 years | 5 | 9 to 10 years | 15 |
| 3 to 4 years | 7½ | 11 to 12 years | 17½ |
| 5 to 6 years | 10 | 13 years and over | 20 |

It is the understanding of this administration that the reference to "cinchona alkaloids" includes the commonly used salts of these alkaloids.

The Council states that in making this recommendation it recognized that 20 grains of the cinchona alkaloids a day do not provide the optimum dose for adults—which should be 30 grains—but that the minimum of 20 grains is specified as a compromise to provide for an effective dose and to conserve the stocks of these alkaloids during the war period.

The Council has expressed the opinion also that the cinchona alkaloids are not effective in the prophylaxis of malaria.

In its enforcement program the Food and Drug Administration will be guided by this authoritative expression of opinion and will regard as misbranded preparations of cinchona alkaloids offered for the treatment of malaria which, when consumed in accordance with the directions in their labelings, provide less than the dosages specified.

The administration heretofore has expressed the opinion—and takes this occasion to emphasize it—that directions for use, to be adequate, should include instructions to repeat the treatment if a relapse occurs.

It has been noted that cinchona alkaloids and preparations of them are sometimes marketed in packages which do not contain amounts of the active principles sufficient to constitute a complete treatment in accordance with the aforementioned schedule. Consideration should be given to the possibility of deception, in violation of the Federal Food, Drug and Cosmetic Act, resulting from the sale of a package labeled to indicate that it contains a treatment for malaria, if the amount of medication supplied in the package is insufficient for that purpose.

Some preparations of the cinchona alkaloids offered as malaria medicines contain active amounts of cathartic drugs. There appears to be no rational basis for such a combination. Some patients suffering with malaria may not need a cathartic. Those who may need such additional medication should base the dosage on the need for it; in other words, the amount of the cathartic administered should not depend on the need for the cinchona alkaloids. There is no objection to advising purchasers to use some suitable cathartic drug in connection with the malaria treatment if constipation occurs.

This notice supersedes the press release of Jan. 3, 1929 entitled "Malaria Preparations Must Comply With Food and Drugs Act Say Federal Officials," issued by the Office of Information, United States Department of Agriculture.

W. G. CAMPBELL,
Commissioner of Food and Drugs.

## RADIO BROADCAST ON SUPPLY OF PHYSICIANS

On Sunday, August 30, from 11:05 to 11:30 a. m. eastern time (10:05 to 10:30 central, 9:05 to 9:30 mountain, 8:05 to 8:30 Pacific time), the Columbia Broadcasting System will air a program entitled "The American Doctor Goes To War." Participants in that broadcast will be Dr. Frank H. Lahey, Chairman, Procurement and Assignment Service of the War Manpower Commission; Dr. Warren F. Draper, Acting Surgeon General, United States Public Health Service (Surg. Gen. Thomas Parran will be on his way to South America); Major Gen. James C. Magee, Surgeon General, United States Army, and Rear Admiral Ross T. McIntire, Surgeon General, United States Navy and personal physician to President Roosevelt.

The representatives of the three services will state their needs, objectives and the current state of achievement toward those objectives—Army, Navy, civilian. Dr. Lahey will represent the point of view of the profession and of the War Manpower Commission in the recruitment and placement of physicians essential to all three fields.

The hour at which this broadcast will occur is a regular talk hour on the Columbia Broadcasting System and has a large station list and a well built up audience. This is the first time that the three services have appeared together on a program of this type. The discussion will not only include the problems of recruitment but provide background as to the type of service rendered in connection with the respective services—military and navy programs.

It is a program which will be of interest not only to doctors and their families but to every family with a relative in the armed services and to every industrial worker or civic leader who ever finds occasion to discuss this problem as a citizen.

## NAVY MEDICAL HEADQUARTERS MOVED

Over the August 14-17 weekend the Bureau of Medicine and Surgery, Navy Department, Washington, D. C., was moved from quarters it had occupied in the Navy Department building to the naval reservation a half mile westward on Constitution Avenue which formerly was the home of the Naval Medical Center. For the first time since outbreak of the war, all divisions of the bureau are together, on the same grounds if not under the same roof. The group of buildings, once the Medical School, Dental School, Hospital and sick officers' quarters, will be known collectively henceforward as Potomac Annex, Navy Department. Since last spring the National Naval Medical Center has occupied its modern new establishment at nearby Bethesda, Md.

## AVIATION PHYSIOLOGISTS

A class in aviation physiology graduated at the School of Aviation Medicine in Texas, August 8, and another class began the course of training on August 10. Among those in the class graduated were Capt. Hayden C. Nicholson, Ann Arbor, Mich., and Lieuts. Halsey G. Bullen, Brooklyn, and Richard L. Masland, Philadelphia, of the medical department, and a number of members of the Air Corps.

Among those in the class beginning August 10 were the following lieutenants of the medical department: Lewis E. Barrick, Chicago; Dale D. Dickson, Letts, Ind.; Vincent H. Handy, East Orange, N. J.; John M. McIver, Cleveland, and various officers of the Sanitary and Air Corps.

The course in aviation physiology treats of the effects of lowered barometric pressure on personnel, anoxia and the effect of flight on man, the operation of low pressure chambers, the theory and practical use of oxygen equipment and the conduct of high altitude indoctrination and classification.

## UNITED CHINA RELIEF COMMITTEE

The president of the Chicago Medical Society, Dr. Oscar Hawkinson, has appointed a committee to represent the medical profession in the Cook County, Ill., campaign for the United China Relief. This committee, comprising Drs. Frank P. Hammond, chairman, Wilbur E. Post, James G. Carr, George W. Post and James H. Hutton, in appealing for funds, points out that doctors, nurses and medical technicians have been the backbone of the famous and unique "American Expeditionary Force in China" and have been credited with sustaining Chinese morale and defeating Japanese propaganda through five years of war in China. Money is desperately needed at once, the committee says. Checks should be made out to United China Relief, Inc., and mailed to this committee at the offices of the Chicago Medical Society, 30 North Michigan Avenue, Chicago.

## LOUISIANA UNIT TO GO ON FOREIGN SERVICE

The Louisiana State University Unit (General Hospital No. 64), which was mobilized for active duty in the army in July, will be assigned to foreign duty, according to B. I. Burns, dean of the Louisiana State University School of Medicine, New Orleans. All medical members of the unit are on the faculty of the medical school; many of them were already on active duty when the unit was mobilized but have since joined the unit. The unit was organized in 1940 by Dr. Urban Maes, who served in France in the surgical section of Base Hospital No. 24 in the first world war. The present unit previous to mobilization was directed by Lieut. Col. Ben R. Heninger, clinical professor of medicine, and now chief of the medical section of the unit. On mobilization, Col. Daniel B. Faust of the regular Army Medical Corps was assigned to command. The chief of the surgical section is Lieut. Col. Charles J. Miangolarra, clinical assistant professor of surgery.

## AMERICAN RELIEF SUPPLIES ARRIVE IN RUSSIA

Russian War Relief, Inc., with headquarters at 11 East 35th Street, New York City, announced on August 9 that a radiogram from Moscow authorities acknowledged receipt of four shipments of relief supplies sent by Americans. The shipments contained medical and surgical supplies, men's clothing, small kerosene stoves, cigarets and other supplies. It was reported that the goods had been distributed to both the army and "the population which has suffered from the German invasion." The kerosene stoves, it was said, "are most valuable for field hospitals." One of the shipments reported received was contributed during a recent "Fill the Ship" campaign for Russian War Relief in southern California.

## TWO DOCTORS APPOINTED FOR WAACS

The War Department recently announced the appointment of two "on contract" surgeons for the Women's Army Auxiliary Corps now stationed at Fort Des Moines, Iowa. They are Dr. Mary L. Moore of Rifle, Colo., and Dr. A. Elizabeth Garber of Chicago. Secretary of War Stimson said at a press conference recently that the WAACs eventually would have women doctors assigned to them full time but that, while the corps is getting its full strength, appointments would be on a contract basis.

## MEDICAL OFFICER AT TRAINING SCHOOL

Lieutenant Commander Hubbard P. Saunders, president of the Chicago Medical Society, has been named the medical officer at the naval training school for electricians mates just opened on the campus of the Kentucky State Teachers College, in Moorhead. He is one of the officers in charge of six hundred navy enlisted men who have been selected for special electrical training before they are sent to do sea service with the fleet. The new school is staffed with six officers.

## FLIGHT SURGEONS' ASSISTANTS

Graduation exercises were held for flight surgeons' assistants who completed the course of training at the School of Aviation Medicine, Randolph Field, Texas, August 1. Certificates were presented by Major Merrill J. Reeh, M. C. General courses for flight surgeons' assistants are conducted annually at the School of Aviation Medicine.

# ORGANIZATION SECTION

## MEDICAL LEGISLATION

### DISTRICT OF COLUMBIA

*Bill Introduced.*—H. R. 7493, introduced by Representative Randolph, West Virginia, proposes to amend the healing art practice act to authorize the issuance of temporary permits to practice the healing art in the District of Columbia, such permits to terminate automatically and become null and void six months after the termination of the present war. Each applicant for a temporary permit will be required to submit satisfactory proof to the commission on licensure that he is over 21 years of age, of good moral character and "has had sufficient professional training and experience to warrant the issuance of said permit." An applicant for such a temporary permit will apparently not be required to possess the qualifications demanded of applicants who apply for permanent licenses.

### MEDICAL BILLS IN CONGRESS

*Bills Introduced.*—S. 2714, introduced by Senator La Follette, Wisconsin, proposes a plan in which vocational rehabilitation will be provided for individuals suffering from war connected or other disabilities. Representative Barden, North Carolina, has introduced the same bill in the House as H. R. 7484. To be known as the War Disabled Vocational Rehabilitation Act, this legislation provides that vocational rehabilitation means the rendering of a disabled individual fit to engage in a remunerative occupation and his placement in employment, including, where needed, physical restoration or repair, medical examination and care, prosthetic and other devices, physical and occupational therapy, training, placement in employment and other appropriate services. This program will be administered by the administrator of the Federal Security Agency. S. 2690, introduced by Senator Reynolds, North Carolina, proposes to strike from the National Defense Act all reference to a Medical Administrative Corps and in the place of that corps to create a Pharmacy Corps in the Army to consist of seventy-two officers. S. 2727, introduced by Senator Schwartz, Wyoming, proposes that any person who is discharged from the active military or naval service for disability incurred in such service in line of duty shall be entitled to domiciliary care in a Veterans' Administration facility pending the adjudication of a claim for disability pension. H. R. 7499, introduced by Representative Lane, Massachusetts, proposes to authorize the President of the United States to issue an appropriate medal and ribbon to be awarded to designated members of the armed forces of the United States during the World War, who, in the interest of humanity and science, acted as voluntary subjects for experimentations during the trench fever investigations in France.

## WOMAN'S AUXILIARY

### Arizona

The Maricopa County medical auxiliary attended a pot luck luncheon on May 6 in the home of Dr. and Mrs. George Irvine of Tempe. The new officers elected were: president, Mrs. James R. Moore; first vice president, Mrs. Paul Case; second vice president, Mrs. Louis Jekel; secretary and treasurer, Mrs. R. W. Hussong, all of Phoenix. Mrs. Harlan P. Mills, president-elect of the Woman's Auxiliary to the Arizona Medical Association, gave suggestions for auxiliary activities for the coming year. Members were urged to work during the summer in the surgical dressing department; 27,000 dressings were made during the past three months in the auxiliary room.

### Arkansas

The Woman's Auxiliary to the Arkansas Medical Society opened its eighteenth annual meeting in Hot Springs, April 27. The general session was called to order by Mrs. E. L. Thompson, Hot Springs, president of the auxiliary to the Garland County Medical Society; invocation was given by Mrs. H. King Wade; the address of welcome was given by Mrs. George B. Fletcher of Hot Springs, and the response to the address of welcome was given by a past president, Mrs. C. E. Kitchens of De Queen. Mrs. Calvin Churchill, state president, was introduced by Mrs. E. L. Thompson. Mrs. J. U. Reaves of Mobile, Ala., president of the auxiliary to the Southern Medical Association, addressed the meeting.

At the open meeting Monday night talks were given by Mrs. Reaves, Colonel Beck and Governor Adkins.

The general session on Tuesday was addressed by Dr. H. Fay Jones, president of the Arkansas Medical Society. The following officers for 1942-1943 were elected: president, Mrs. L. G. Fincher, El Dorado; president-elect, Mrs. L. J. Kosminsky, Texarkana; first vice president, Mrs. Euclid Smith, Hot Springs; second vice president, Mrs. H. T. Smith, McGehee; third vice president, Mrs. L. F. Barrier, Little Rock; fourth vice president, Mrs. J. K. Walker, Pine Bluff; treasurer, Mrs. Sam Thompson, Camden; parliamentarian, Mrs. Fount Richardson, Fayetteville; historian, Mrs. C. W. Garrison, Little Rock; publicity secretary, Mrs. M. E. Foster, Fort Smith. The auxiliary voted to create the office of poet laureate and elected Mrs. Fletcher.

At a luncheon Mrs. William Hibbitts, national program chairman, gave an interesting talk, and Mrs. C. W. Garrison installed the new officers. The new president, Mrs. Fincher, delivered an address and presided over the board meeting which followed the luncheon.

### District of Columbia

At the annual meeting of the Woman's Auxiliary to the Medical Society of the District of Columbia the results of the year's membership drive were reported. One hundred and three new members were added, making the active members three hundred and twenty-eight and associate members thirty-five.

Besides collecting more than $1,700 during the Red Cross membership drive, the membership has contributed more than eight thousand hours in rolling bandages, knitting, sewing and the like for the Red Cross. Members have also prepared themselves for assistance in defense work by taking all types of courses given by the Red Cross and other organizations.

### Mississippi

The quarterly meeting of the auxiliary to the Northeast Mississippi Thirteen Counties Society was held at the home of Mrs. A. E. Brown in Columbus June 9. Mrs. Stanley A. Hill, Corinth, presided. Mrs. V. B. Philpot, Houston, state president, reported on the state meeting. Mrs. W. J. Aycock, councilor, urged the doctors' wives of unorganized counties to engage in auxiliary work. The wives of Lowndes County announced their intention to organize the following week. Mrs. Edward Slaughter of Columbus, the guest speaker, discussed nutrition and the preparation of foods.

### Pennsylvania

The Lycoming auxiliary met at Williamsport on April 10. On the advice of the advisory committee of the medical society, the auxiliary voted to purchase a microprojector for the Williamsport Hospital at a cost of about $250. A letter was read by Mrs. Carl H. Senn, treasurer, acknowledging receipt of $200 for the Medical Benevolence Fund.

# *Medical News*

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

## CALIFORNIA

**Personal.**—Dr. Jacob C. Geiger, San Francisco, has received the blue ribbon and collar of the Order of Merit, grade of commander, of the government of the Republic of Chile, South America, "for excellence of administration and research in solving public health problems."

**Course for Sanitarians.**—The department of bacteriology at the University of California, Berkeley, opened a special training course for sanitarians on August 7 to continue until October 3. Topics to be covered include public health administration and organization, communicable diseases and their control, general epidemiology and vital statistics, and sanitation and sanitary inspection. The course will include lectures, seminars, laboratory practice and field trips covering the theoretical and practical aspects of the sanitation program being given at the request of state public health officials.

**Surgical Impostor Sentenced.**—Arthur Osborne Phillips, alias Dr. James Herman Phillips, was sentenced on June 29 to nine months in the county jail at Oroville. According to newspaper reports, Phillips had pleaded guilty to a felony charge of possessing a concealed weapon. Phillips' sentence will run concurrently with a six month sentence imposed when he was convicted of charges of practicing medicine without a license, according to an Associated Press dispatch. On May 26 Phillips had been charged with impersonating a surgeon and performing operations without a license in a hospital in Chico. He is reported to be the same Phillips who in 1932, using the same alias, masqueraded as a surgeon in Alabama and later was sentenced to the Alabama state prison for practicing without a license.

## CONNECTICUT

**Physician Honored.**—The Norwalk Medical Society gave a dinner recently for Dr. William J. Tracy, Norwalk, who has served the community for fifty years. Dr. Charles Gordon Heyd, New York, was the principal speaker. Dr. Tracey was presented with a set of three volumes bound in leather on surgical technic and a set of metal book ends.

**New Maternity Wing at Hartford Hospital.**—The six story maternity wing of the new five million dollar Hartford Hospital was dedicated on July 9. The two lower floors of the new unit will be for outpatients, the next three for inpatients and on the top floor will be a delivery suite. There are nurseries on each floor. Of the three inpatient floors the top will be for private single rooms, the middle for semiprivate rooms and the lowest for four and eight bed wards.

## DISTRICT OF COLUMBIA

**Survey on Disease Immunity.**—Plans to conduct a house to house canvass to determine the immunity status of the population are under consideration by the District Health Department and the civilian defense mobilization division, the Washington *Post* reported on August 13. At the conclusion of the fact finding campaign an immunization drive will be inaugurated. The house to house canvass will be done by volunteer workers of the civilian mobilization unit, it was stated.

## GEORGIA

**Society Sponsors Public Lectures.**—The Fulton County Medical Society, Atlanta, recently sponsored a series of public lectures. The first lectures were given by Dr. Julian L. Rawls, Norfolk, Va., on "The Physician's Duty in Time of War"; Col. Sanford W. French, Fort Leavenworth, Kan., "Medical Care of the Soldiers," and Dr. James E. Paullin, Atlanta, president-elect of the American Medical Association, "Medical Care of the Civilian Population in War." A symposium on cancer with Drs. Charles E. Rushin, John F. Denton, Calvin B. Stewart and Eustace A. Allen, all of Atlanta, as the speakers constituted the second group of lectures. Two moving pictures on nutrition and a talk by Rev. Louie D. Newton, pastor of Druid Hills Baptist Church, Atlanta, on "The Great Physician," concluded the series.

## ILLINOIS

**Posthumous Award of Silver Star.**—Capt. Charles A. Stafford of Hinsdale and the U. S. Army Medical Department was cited for "devotion to duty and coolness under fire." Captain Stafford, who was killed on March 3, was posthumously awarded the army silver star for gallantry in action during the evacuation of Java.

## IOWA

**Personal.**—Dr. John McDannell, Nashua, was recently made a member of the Iowa State Medical Society's fifty year club, having completed fifty years in the practice of medicine.

**Society News.**—Dr. Robert M. Collins, Council Bluffs, addressed the Taylor County Medical Society recently in Lenox on "Modern Use of Hormones in Obstetric and Gynecologic Practice."——The Lee County Medical Society was addressed in Keokuk, June 24, by Drs. John Harry Murphy and William L. Sucha, both of Omaha, on "Diagnosis and Treatment of Tuberculosis in Childhood" and "Diagnosis and Treatment of Surgical Shock" respectively.——Among others, Drs. Richard Charles Adams and Austin C. Davis, both of Rochester, Minn., addressed the Upper Des Moines Medical Society in Spirit Lake, August 6, on "Anesthesia in Rectal Surgery" and "Endocrinologic Diagnosis in General Practice," respectively.

## INDIANA

**Personal.**—Dr. Maurice Joseph Barry was elected president of the Indianapolis Board of Health, July 17, succeeding Dr. George W. Kohlstaedt, whose term expired June 1.——Dr. Hubert B. Pirkle, resident physician at the Indiana State Sanatorium at Rockville, has been named acting superintendent during the absence of Dr. Robert A. Staff, Richmond, who is with the armed forces.

**The Oberlin Award.**—The Lake County Medical Society has established the Oberlin Award in memory of the late Dr. Thomas W. Oberlin of Hammond, one of the society's charter members. The award will be presented each year to a Lake County citizen or institution making the greatest contribution to the health of the people of Lake County. It will be given in the form of a plaque on which will be engraved the name of the recipient, the year of presentation and "presented by the Lake County Medical Society in recognition of significant contributions to the health and consequent welfare, security and happiness of the people of Lake County." The award will be given each year at the annual meeting of the society. The recipient will be selected by a permanent Oberlin award committee to be named by the council of the society.

## KANSAS

**Sedgwick County Essay Contest.**—The Sedgwick County Medical Society is offering a fifty dollar cash prize to members and intern members of the society, the essay to be submitted to the society not later than October 1. The prize winning essay should be on original work accomplished while a member of the society or while an intern member of the society. It is to be read before the medical society at its December meeting.

## KENTUCKY

**Director of Maternal Welfare Resigns.**—Dr. Charles B. Crittenden, Louisville, resigned on July 2 as director of the division of maternal and child welfare of the state health department on account of ill health. Dr. Alice D. Chenoweth, formerly of Rosemont, Pa., has been named to succeed Dr. Crittenden.

**Changes in Health Officers.**—Dr. James O. Nall, Marion, has resigned as health officer of Livingston County to accept a district appointment in Crittenden, Caldwell and Lyon counties. He has also resigned as secretary of the Livingston County Medical Society. The health unit has been combined with the one in Marshall County with Dr. Samuel L. Henson, Benton, as full time health officer.

## LOUISIANA

**Fellowships in Tropical Medicine.**—The American Foundation for Tropical Medicine, Inc., announces the establishment of two paid fellowships at the Graduate School of Tropical Medicine of Tulane University of Louisiana, New Orleans. The fellowships have been made possible by the Winthrop Chemical Company, Inc., Winthrop Products, Inc., and the Lambert Pharmacal Company of St. Louis. These fellowships, which will be known as the Winthrop Fellowship and the

Lambert Pharmacal Co. of St. Louis, Mo., fellowship, have been established to provide graduate training in tropical medicine for young physicians who are citizens of the United States. Applications should be addressed to the dean of graduate studies, Tulane University, New Orleans. According to an announcement the exact names of the fellowships should not be altered, since the phraseology in each instance has been designated by the donor.

## MARYLAND

**Dog Quarantine in Baltimore.**—A quarantine on dogs was established by the state board of agriculture for northwest Baltimore and adjoining areas in Baltimore County, effective June 11 to September 11, following the discovery of rabies in dogs in the county near the city boundary. This is the first time that such an action has been taken in Baltimore. Until recently there had been no known rabid dogs in the Baltimore area since 1931.

**Dr. Colston Succeeds Dr. Hugh Young.**—Dr. John A. C. Colston, since 1934 associate professor of urology at Johns Hopkins University School of Medicine, Baltimore, has been announced as the successor of Dr. Hugh H. Young as professor of urology at Johns Hopkins and as director of the Brady Urological Institute of Johns Hopkins Hospital. Dr. Young retired on June 30 with the title professor emeritus of urology. Dr. Colston was born in Baltimore in 1886, graduated at Johns Hopkins in 1911 and has been a member of the staff since 1915.

## MASSACHUSETTS

**Dr. Elkind Resigns from Mental Hygiene Society.**—Dr. Henry B. Elkind, Boston, has resigned as medical director of the Massachusetts Society for Mental Hygiene, effective August 12, to enter active service in the medical corps of the army. Dr. Elkind has been medical director of the society since 1925.

## MICHIGAN

**Government Buys Battle Creek Sanitarium.**—The Battle Creek Sanitarium has been turned over to the government and will in the future be known as the Percy L. Jones General Hospital for war casualties. The purchase price was more than two million dollars. Col. Norman T. Kirk, M. C., U. S. Army, will head the hospital. The first patients will arrive about October 1 from military training centers where they have contracted ailments requiring long treatment. The former patients of the sanitarium have been transferred to several nearby buildings to continue treatment under the general direction of Dr. John H. Kellogg of Battle Creek, it was announced.

**Clinic Awards Prizes for Essays.**—The first prize of $100 in the essay contest at the North End Clinic, Detroit, was won by Dr. Jerome Mark, Detroit, whose subject was "Venography: A. Its Use in the Differential Diagnosis of the Peripheral Venous Circulation. B. A Simplified Technic." Second prize of $75 went to Dr. Aaron A. Farbman, Detroit, for his paper on "The Effect of Estrogenic Hormone on Hyperthyroidism." Honorable mention was given to Dr. Ezra Lipkin, Detroit, for his paper on "Brachial Plexus Block in the Treatment of the Painful Shoulder—A Review of Fifty Cases." The contest is held to promote the study of end results in the treatment of cases at North End Clinic and to encourage clinical and experimental research.

## NEW JERSEY

**Outbreak of Poliomyelitis.**—Two deaths have occurred among 11 cases of infantile paralysis in Elizabeth, according to the New York *Times*, August 4. The 11 cases had been reported to the state department of health since July 1.

**Health Board Abolishes Eye Clinic.**—On June 23 the Clifton Board of Health voted unanimously to abolish the eye clinic of the board as a measure of economy. The clinic has been under attack repeatedly by the committee for the control of blindness of the Passaic County Medical Society because it was directed by an optometrist and not a licensed physician. According to the Bulletin of the Passaic County Medical Society, Clifton school physicians refused to refer school children to the clinic and the attendance dropped sharply.

**Society News.**—Dr. Leon Herman, Philadelphia, addressed the Cumberland County Medical Society, June 9, at Bridgeton, on "Difficulties Encountered in the Interpretation of Genitourinary Symptoms."——Dr. George T. Pack, New York, discussed "Early Diagnosis and Management of Carcinoma of the Stomach" before the Bergen County Medical Society recently in Bergen Pines.——The Gloucester County Medical Society was addressed in Woodbury recently by Dr. Herbert T. Kelly, Philadelphia, on "Nutrition as It Applies to General Disease."

## NEW YORK

**Food Poisoning from Cream Pie.**—Twenty employees of an upstate industrial plant were reported ill with food poisoning in an outbreak traced to contaminated cream pie. The illness was characterized by nausea, vomiting and diarrhea. Some of the patients experienced profuse sweating, abdominal pain, bloody stools and shock. The onset was sudden, with recovery from acute effects within twenty-four to forty-eight hours. There were no fatalities. According to *Health News*, all twenty employees had eaten the last meal prior to the development of the illness at the plant cafeteria. Cream meringue pie was the one food that was consumed by all the patients. The first person who became ill ate a portion of the pie about 5:30 p. m. on June 12 and had onset of symptoms about 9 o'clock that evening. Those who partook of the pie later had a shorter incubation period and those that ate it at 3 a. m. on June 13 became ill within two hours. Examination of the pie demonstrated heavy contamination of both the cream filling and the meringue with Staphylococcus aureus. The pies were prepared about midnight, June 11-12, and were about 18 hours old when the first patient was served. It was definitely established that no food handler in the kitchen was ill but that contamination was caused by insanitary cleaning practices.

### New York City

**New Secretary of Board of Health.**—Dr. Frank A. Calderone, instructor in preventive medicine at the New York University College of Medicine, has been appointed secretary of the New York City Department of Health to succeed Goodhue Livingston Jr., who has resigned for war duty. Dr. Calderone graduated at New York University in 1924 and since 1938 has been serving as district health officer of the lower east side.

**Proposed Program to Rehabilitate Blind.**—The New York Association for the Blind recently presented to government authorities for consideration a plan for the rehabilitation for war blinded. The plan would seek to reach the blind service man at the hospital bedside and follow through with a program of readjustment. The New York Association for the Blind recommended the creation of a division for the blind in the U. S. Employment Service.

## OHIO

**Opposition to Insurance Plans Set Up.**—Newspapers have announced that an organization has been set up in Cleveland to develop opposition to medical service insurance plans in the community. The group will be known as the Association for Preservation of the Present American System of Medical Practice. Officers during the organization period include Drs. Carl L. McDonald and Theron S. Jackson, co-chairmen; Dr. John Robert Andrews, vice chairman; Dr. David M. Keating, secretary, and Dr. Max B. Laven, treasurer, all of Cleveland. According to the Cleveland *News* the association has as its only purpose the defeat of the proposed medical plan of insurance and favors the freezing of medical practice in its present status until after the war. Creation of this group followed the recent organization of the Cleveland Medical Service Association, which is a cooperative project of certain members of the Academy of Medicine of Cleveland.

## PENNSYLVANIA

**Society News.**—The Reading Eye, Ear, Nose and Throat Society was addressed by Dr. Nevin H. Rupp, Reading, July 15, on "Eye, Ear, Nose and Throat Aspects of Chemical Warfare."——Dr. James O. Wallace, Pittsburgh, discussed "Management of Infantile Paralysis" before the Cambria County Medical Society in Johnstown, July 9.

### Philadelphia

**Health Commissioner Visits England.**—Dr. Hubley R. Owen, director of public health, recently went to England "to make a first hand observation in the fields of civilian defense and public health in wartime," newspapers report.

**Changes at University of Pennsylvania.**—Dr. Paul C. Colonna, director of orthopedics of the State University and Crippled Children's Hospital, and professor of orthopedic surgery of the University of Oklahoma School of Medicine, Okla-

homa City, has been appointed professor of orthopedic surgery at the University of Pennsylvania School of Medicine. Other changes on the faculty include the appointment of Harry E. Morton, Sc.D., to associate professor of bacteriology, Dr. Dale R. Coman to assistant professor of pathology, Richard G. Abell, Ph.D., to assistant professor of anatomy, Dr. Oscar V. Batson to professor of anatomy in the Graduate School of Medicine and assistant professor of otolaryngology in the school of medicine, and Dr. Harriett Elizabeth Glenn Ravdin to assistant to the dean, school of medicine.

**Cancer Council Sponsors Program for Teachers.**—The Philadelphia Cancer Council has arranged a program for high school science teachers at the Philadelphia County Medical Society, October 20, aimed to show how a special subject, in this instance cancer, can be used to tie together physics, mathematics, chemistry, biology and the other science subjects that are taught in high schools. The program will open with Dr. William Bates, president of the Philadelphia County Medical Society, presiding, and speakers will be Dr. Stanley P. Reimann, chairman of the cancer commission of the state medical society, on "Use of a Correlating Subject in Science Teaching," and Oscar Riddle, Ph.D., department of genetics, Carnegie Institution, Cold Spring Harbor, N. Y., "Biology In and Not In the High School." Robert W. Kunzig, president of the Science Teachers Association, will close the discussion.

## TENNESSEE

**Radiologists Elect Officers.**—Dr. Horace D. Gray, Memphis, was elected president during the recent annual meeting of the Tennessee Radiological Society in Memphis. Other officers are Drs. Franklin B. Bogart, Chattanooga, vice president, and John Marsh Frere, Chattanooga, secretary-treasurer.

**Changes in Health Personnel.**—Dr. Francis H. Cole, Nashville, has been placed in charge of the division of tuberculosis control of the Memphis and Shelby County Health Department, effective July 1. He succeeds Dr. Felix A. Hughes Jr., Memphis, who has been assigned to take charge of Lynnhurst Sanatorium, Oakville.

**New Medical Officer at Marine Hospital.**—Dr. Anthony P. Rubino, formerly of Key West, Fla., of the U. S. Public Health Service, has been appointed medical officer in charge of the United States Marine Hospital, Memphis. He succeeds Dr. Edwin H. Carnes, who was transferred to Alaska. Dr. Rubino has been a member of the public health service since 1926.

## WEST VIRGINIA

**State Society Approves Sickness Insurance.**—The West Virginia State Medical Association, at its annual session in July, went "on record as approving the principle of voluntary insurance to pay sickness costs." The action was the culmination of a four year period of study of the subject. It was recommended, however, that "for the present" there be held "in abeyance the adoption of any statewide plan and support rather the development of medical service plans in local communities having common and similar problems." It was further recommended that "each plan shall provide for a schedule for medical fees at least equivalent to the minimum professional fee schedule adopted by the county medical society in the county or counties in which the plan is organized."

## WISCONSIN

**Dr. Urben Made Director of Mental Hygiene.**—Dr. Walter J. Urben, senior physician at the Mendota State Hospital, Mendota, has been appointed director of the state division of mental hygiene, filling the vacancy caused by the death of Dr. Gilbert E. Seaman, Madison, May 25, 1941. Dr. Urben graduated at the University of Wisconsin Medical School, Madison, in 1930. Before joining the Mendota staff, Dr. Urben was assistant superintendent of the Massillon State Hospital in Ohio, senior physician at the Southern Wisconsin Colony and Training School, Union Grove, and staff physician at the Milwaukee County Hospital for Mental Diseases.

**Borden Prize Awarded to Chemist.**—Hugo H. Sommer, Ph.D., professor of dairy industry, University of Wisconsin, Madison, was presented with the Borden prize of the American Dairy Science Association at its recent annual meeting. The prize consists of a gold medal and $1,000. Dr. Sommer received his degree of doctor of philosophy at Wisconsin in 1922. For a time he was chemist of the North California Milk Producers Association, joining the University of Wisconsin in 1920. His work covered various aspects of dairy chemistry, including the study of the acidity of milk, milk grading, solubility of metals in milk and the curd strength and rennet coagulation of milk in relation to mastitis.

**Society News.**—Dr. Philip S. Hench, Rochester, Minn., discussed "The Management of Rheumatoid Arthritis" before the Medical Society of Milwaukee County in Milwaukee, May 8, and Dr. Walter P. Blount, Milwaukee, spoke on "The Kenny Treatment of Poliomyelitis."——Dr. William G. Lennox, Boston, addressed the Milwaukee Neuro-Psychiatric Society in Madison recently on "Twins, Brain Waves and Epilepsy."——At a meeting of the Milwaukee Society of Clinical Surgery, May 13, in Sheboygan, Drs. Friedrich Eigenberger, Sheboygan, spoke on "The Use of the Polarograph for Laboratory Diagnosis" and Paul B. Mason, Sheboygan, "Preoperative and Postoperative Medical Care of Surgical Patients."——Dr. Ralph E. Campbell, Madison, discussed "Carcinoma of the Uterus" before the Sheboygan County Medical Society in Sheboygan recently. ——Dr. William F. Braasch, Rochester, Minn., addressed the Rock County Medical Society recently on "Advances in the Treatment of Urinary Tract Infections."

## GENERAL

**Dr. Upham Named Chairman of Parenthood Foundation.**—Dr. John H. J. Upham, Columbus, Ohio, formerly President and Trustee of the American Medical Association, was recently chosen president of the board of directors of the Planned Parenthood Foundation of America, Inc.

**Research Chemicals Division Created at Breon and Company.**—The George A. Breon & Company laboratories, Kansas City, Mo., have established a research chemicals division which will prepare synthetic organic chemicals, including bile acids, hormones and vitamins. The catalogue listing these products was recently distributed to research workers in the medical sciences, according to an announcement from the company. The new department will be under the direction of Clarence W. Sondern, Ph.D., Kansas City, and Willard M. Hoehn, Ph.D., formerly of Rochester, Minn.

**Motion Picture on Back Siphonage.**—Pure Water Films, Inc., has prepared a motion picture illustrating the danger to health of faulty plumbing, using a story based on a law suit. THE JOURNAL, August 22, page 1437, announced that this film had been prepared by the Plumbing and Heating Industries Bureau. The picture shows clearly that disease may result from the drinking of polluted water caused by back siphonage of plumbing fixtures. It is available for showing before medical students, medical societies and county health officers. Those desiring to borrow this film may communicate with Mr. William J. Lang, chairman of the Motion Picture Project Committee of the National Association of Master Plumbers, 1251 North Clark Street, Chicago.

**Physicians Reported Missing.**—The following physicians have been reported missing, according to recent newspaper reports:

Lieut. Edward F. Ritter Jr., Mattoon, Ill., M. C., U. S. Navy. Lieutenant Ritter was said to be in service on Corregidor and is believed to be a war prisoner of Japan.

Capt. Robert G. Davis, M. C., U. S. Navy. Dr. Davis was commanding officer of the U. S. Naval Hospital, Canacao, P. I., at the time war was declared.

Capt. Wilbert W. Buckhold, Blackey, Ky., M. C., U. S. Army. Captain Buckhold is believed to have been captured on Corregidor.

Dr. Jacob Markowitz, Toronto, Ont., Canada, missing in the recent operations in Malaya.

Dr. John D. Greathouse, U. S. Navy Reserve, Minneapolis, "lost at sea somewhere in the Pacific." He was in charge of personnel on a Standard Oil Company tanker.

**Grenfell Mission Unveils Anniversary Tablet.**—A tablet was unveiled at St. Anthony, Newfoundland, August 4, to commemorate the fiftieth anniversary of the landing of the late Dr. Wilfred Grenfell on the coast of Labrador. Sir Wilfred established the mission in Labrador in 1892. Since his death on Oct. 9, 1940 the activities of the mission have been carried on under the direction of Dr. Charles S. Curtis, St. Anthony. During the fifty years of Sir Wilfred's missionary work five hospitals have been established there, five nursing stations, two boarding schools, one day school and children's home, social services to improve the lot of the coast people, two hospital ships and a supply ship. The inscription on the new tablet reads "In gratitude to God for the Labrador Doctor." The Grenfell Association of America is located at 156 Fifth Avenue, New York.

**Nutrition Foundation Publishes Journal.**—*Nutrition Reviews* has been established as the official journal of the Nutrition Foundation, Inc., New York, with Dr. Frederick J. Stare, assistant professor of nutrition and biochemistry, Harvard University, Cambridge, Mass., as editor. It will be supervised by an editorial committee representing nutrition research and

medicine. The new journal will appear monthly. The foundation announces that six new member organizations had contributed new subscriptions amounting to $75,000, raising the foundation's fund to support nutrition research to $923,500. The foundation is now supporting thirty-six nutrition research studies in twenty-two leading universities of the nation. These studies are divided equally among three kinds of projects: those having a direct relationship to the war emergency, those having a direct relationship to public health and those that primarily advance the frontiers of the science of nutrition.

**Examination in Ophthalmology.**—The American Board of Ophthalmology announces that the examinations will be held in New York, December 13-16, and Los Angeles, January 15-16, because of the war emergency. It was decided to cancel the 1943 written examination, to include in the oral examination all the subjects previously covered by the written examination and to dispense temporarily with the requirement of case reports. The oral examination will probably require two or three days and will cover external disease, slit lamp, ophthalmoscopy, histology, pathology, bacteriology, ocular motility, refraction, retinoscopy, practical surgery, anatomy and embryology, perimetry, therapeutics and operations, optics and visual physiology and relation of the eye to general diseases. Applications on the proper blanks for the December and January examinations must be filed with the secretary not later than November 1. Blanks may be obtained from the American Board of Ophthalmology, 6830 Waterman Avenue, St. Louis.

**Congress of Physical Therapy.**—The American Congress of Physical Therapy will hold its annual session at the Hotel William Penn, Pittsburgh, September 9-12. A series of instruction courses will be held throughout the entire session. Among the speakers on the program will be:

Stafford L. Osborne, Ph.D., Chicago, Present Status of Electromuscle Stimulation.
Dr. William Cooper, New York, The Problem in Cerebral Palsy.
Dr. Fred Bennett Moor, Los Angeles, The Future of Physical Medicine.
Dr. Paul B. Magnuson, Chicago, Painful Back.
Dr. Harry T. Zunkel, Brooklyn, The Galvanic Bath.
Dr. Ralph Pemberton, Philadelphia, Refinements in the Treatment of Arthritics Including Physical Therapy.
Dr. Christopher J. McLoughlin, captain, U. S. Army, Atlanta, Physical Therapy in Relation to Military Medicine.
Dr. Bengt N. Bengtson, lieutenant commander, U. S. Navy, Great Lakes, Ill., Sustained (or Prolonged) Radiant Heat Therapy in Lesions of the Pelvis.

There will be a symposium on poliomyelitis on Thursday with Drs. John A. Toomey, Cleveland; Jessie Wright, Pittsburgh, and Miland E. Knapp, Minneapolis. A symposium on fever therapy on Friday will be conducted by Drs. Earl C. Elkins, Rochester, Minn.; Herbert Worley Kendell, Dayton, Ohio; Robert F. Dow, Paterson, N. J.; John W. Fredette, Pittsburgh; Frederick M. Allen, New York, and Lyman W. Crossman, New York.

## FOREIGN

**Pasteur Journal Prohibited.**—The Germans have forbidden the publication of the Journal of the Pasteur Institute of Paris, the Chicago *Sun* reported, July 25. The report stated that the journal was founded in 1881 by Pasteur himself.

**Prizes for Encephalitis Research.**—The Foundation at the University of Berne to promote encephalitis research announces its annual prizes for work on encephalitis lethargica showing real progress in the diagnosis or treatment of the disease. The smallest prize amounts to 1,000 Swiss francs. The prizes are awarded at the end of each year. Those wishing to participate in the competition should send their application to the dean of the faculty of medicine at the University of Berne.

**Rockefeller Grant to Nutrition Survey.**—The Rockefeller Foundation has made a grant of £1,875 toward the expenses of the Oxford Nutrition Survey during the past year and has promised a grant of £3,000 for each of the next two years. The funds will be administered by a committee consisting of the regius professor of medicine, the Whitley professor of biochemistry and the Waynflete professor of physiology. According to *Science* the survey is investigating economic, dietary, clinical and biologic methods of assessing nutrition in man. Besides giving training in their use it is also, on behalf of the Ministry of Health, examining the nutrition of samples of the population.

**German Narcotic Law Amended.**—Effective as of July 1, 1941, a decree of the reich minister of the interior subjected the distribution of the following chemicals to the restrictions imposed by the narcotic law of Germany: methylphenylpiperidincarbonic acid-ethyl-ester ("Dolantin"), phenylaminopropane ("Aktedron," "Benzedrin," "Elastonon") and phenyl-methylaminopropane ("Pervitin"). The decree was signed in behalf of the minister of the interior by Dr. L. Conti, who is the leader of the health office of the party and leader of the German physicians (reichsaerztefuehrer). Dr. Conti, it is said, is known to be a very active opponent of habit forming stimulants and to favor a strict enforcement of the narcotic laws and of the laws pertaining to abortions.

## SPECIAL NEWS

(THIS NEWS WAS ASSEMBLED ESPECIALLY FOR USE IN THE JOURNAL)

**Public Health under Hitler's Rule.**—The *Neues Wiener Tageblatt* reports the opening by Gauleiter Dr. Jury of the Central Office for Childless Marriages, which has been set up within the Chief Health Office of the Gau Niederdonau. Among the guests present were Dr. Fehringer, chief of the Gauamt for Racial Policy, SA-Obergruppenführer von Schorlemer, Gauarzteführer Dr. Tangl, Gaufrauenschaftleiterin Anni Victoris Gauhauptmann Dr. Mayer, Generalstabsarzt, Dr. Zimmer, Generalarzte Dr. Zeman and Dr. Albrecht, Prof. Dr. Knoll (rector of Vienna University) and the deans of the medical and philosophical faculties, Professor Pernkopf and Professor Christian. Dr. Fehrenger said that is the aim of the central office to provide biologically sound but hitherto childless married couples with all the resources of medical art to remove infertility and also to insure that married couples will not have to forego treatment simply because they cannot afford the expense. After the war the present institute would develop into an institute for research into human fertility. Dr. Jury said "I am glad that it was my gau in which it has been possible to set up the first central office for childless marriages, and I believe that it will prove not only important for the war but also important for the reich (reichswichtig).

DNB reported that Schirach paid a surprise visit to a number of camps of the child evacuation scheme in the Harz area, where children from northwest German towns which are particularly exposed to, or have particularly suffered from, air raids have been staying for some months. The condition of all camps was irreproachable. The health of the children was incomparably better than on their arrival, thanks to the favorable position of the camps and the very ample food. Parents recently visited all the camps.

The *Deutsche Zeitung*, Budapest, notes that a thousand rooms have been reserved for wounded Hungarian soldiers in various bathing resorts on Lake Balaton.

The Scandinavian Telegram Bureau reports from Rome that at Bari a military tribunal has sentenced nine military doctors, twelve civilians and twenty-three soldiers to long terms of imprisonment for illegal traffic in health certificates. For payment the doctors procured sick leave permits and in some cases exemption from military service. The doctors were sentenced to terms of imprisonment ranging between seven and twelve years, the soldiers from six to seven years and the civilians up to fourteen years.

The *Revaler Zeitung* reports that the villages of Illurma and Walkse in the Keila parish, Estonia, are declared to be menaced by rabies.

The Berlin correspondent of the *Aftonbladet* quotes the annual review of the Central Bureau of Statistics as calling for a rise of 60 or 70 per cent in the German birth rate "to put the German people in a position to deal with the tremendous tasks awaiting them." The number of families with three children or less has risen since 1933 by 1,700,000, while in the same period the number of large families has diminished by 80,000.

The *Völkischer Beobachter*, in an editorial by Fritz Nonnenbruch, advocates the necessity of increasing the birth rate. "We Germans will become a herrenvolk, and have never before in our history felt the call to become a herrenvolk more strongly than now. The task of a healthy herrenvolk—in contrast to a parasite people—does not consist in enjoying life. Our people's task is more serious, greater and more far reaching. A herr is a person who can be what he is, who develops his mind and characteristics freely. Therefore a herrenvolk is a people that develops its mind and characteristics freely. Our postwar tasks consist in exhausting the immense possibilities which our soldiers' victory opens up to us; this in the first place involves, literally speaking, growing into these possibilities as far as figures are concerned. The greater reich's greater tasks demand a greater people."

# Foreign Letters

## LONDON

*(From Our Regular Correspondent)*

July 18, 1942.

### Polish Medical Journal Published in England

There are many Polish refugees in this country, the majority of whom are soldiers. The foundation of a Polish Faculty of Medicine in Edinburgh University has been described previously (THE JOURNAL, January 24, p. 313). After a lapse of two years the Poles have continued in England publication of their only surviving medical periodical, the *Lekarz Wojskowy*, the Journal of the Polish Army Medical Corps. Its object is to describe the experience gained by Polish doctors during the war and to facilitate contacts of the Polish medical circle with the wide English speaking medical world. The periodical is in its thirty-fourth volume and has published in England three numbers. The articles are in Polish, but summaries in English are added. In an attempt to excuse their barbarity the Germans have pretended, with their usual effrontery, that the Poles have no civilization worthy of the name. The pages of the *Lekarz Wojskowy* certainly do not support this aspersion, for the articles are of an unusually high standard. In one entitled "A Theory of True Uremia" A. Fidler points out that the theory that uremia is due to impaired renal function lacks proof, namely diminution of nonprotein nitrogen in the urine. Investigations at the University of Warsaw showed that the amount is slightly increased over that in health. Hence arose the idea that the retention of nonprotein nitrogen is due to the breakdown of proteins in the blood and tissues. This was confirmed by demonstrating that the proteins of the serum are altered in their physicochemical structure and so are liable to break down, which leads to the conclusion that uremia is a disease of the blood rather than of the kidneys.

B. Hejduk deals with "The Organization of Field Surgery in Modern War." Such is the enemy that he has to write "Large unprotected hospitals far behind the front have not proved satisfactory, as they can easily be bombed." The evacuation of hospitals by ambulance trains has failed, as the lines are frequently damaged. Work is now possible only in small, well protected hospitals. Operation theaters and wards are installed in underground shelters, such as wine cellars and crypts.

Prof. D. Cordier discusses "Anoxemia in Traumatic Shock." He holds that anoxemia probably plays the most important part and that therefore the sooner oxygen therapy is used the better.

H. Back deals with avitaminosis in the army. A large part of the vitamins is lost in the intensive army cooking. Vitamin A deficiency may be produced and shown by sporadic night blindness. Vitamin C deficiency is shown by inflammation of the gums and eczema.

### Medical Supervision of the Young After Entering Industry

The history of the medical profession in this country in recent years can be summed up in three words—increased state control. The London Regional Advisory Council for Juvenile Employment has made the latest proposal in this direction in a memorandum submitted to the Ministry of Labor and National Service. The council assumes that the school leaving age will be raised from 14 to 15 and possibly to 16 years and that compulsory day continuation classes will be set up for juveniles beyond the age for leaving school. The council recommends an extension of the school medical service to all minors in industry by an arrangement which would empower the medical staff of the local authority to supervise, even where it did not itself provide, all medical treatment, including psychotherapy, from nursery school to the end of adolescence in industry.

### Delayed Union of Fractures

Delayed union of fractures was discussed at a meeting of the British Orthopedic Association on the basis of war experience, in which American and Canadian surgeons on duty in this country took part. Mr. R. Watson-Jones and Squadron Leader W. D. Coltart presented an analysis of five hundred fractures of the shaft of the femur or tibia treated in the orthopedic units of the Royal Air Force. The most important factors responsible for delayed union were (1) infection, (2) distraction of the fragments by excessive skeletal traction and (3) delayed reduction, late manipulation and, in the femur, late bowing or refracture. In the absence of these delaying causes, union was firm enough for removal of splints or plaster in an average of fourteen weeks. When minor angulation remained, early resumption of weight bearing in a walking plaster constituted a delaying factor. This, by increasing the angulation momentarily, distracted the fracture on its open side. If the cause of the delay was recognized and the period of plaster immobilization extended, the result was slow union.

Prof. Harlan E. Wilson of the U. S. Public Health Service believed that the type of initial violence might account for the greater time taken for motorcycle injuries to heal. The speed of impact was noteworthy. Damage to the vascular supply of bone influenced greatly the time of healing. Multiple fractures, by making greater demands on the osteogenic functions, accounted for the frequency of delayed union in these cases.

Major A. W. M. White of Toronto said that the factors most likely to affect the rate of union were apposition of the fractured surfaces and complete and continuous immobilization. In fifty-one well reduced and immobilized legs the average time for union was four and a quarter months; in thirteen inadequately reduced or poorly immobilized cases it was eight and a quarter months.

## PARIS

*(From a Special Correspondent)*

July 4, 1942.

### Growth Vitamins and Alimentation

After nearly two years of alimentary restrictions the most urgent problem for the physicians of France consists in observing children. The growth of children, their physical and psychic development, is now the greatest biologic problem.

Charles and Gabriel Richet, members of the Académie de médecine, have written a book on the problems of puberty and adolescence which is soon to be printed. They published a chapter of the book called Biologic Growth Value of Aliments in the *Paris médical*, January 30. The authors discuss the amino acids of growth and the growth vitamins. The American authors Osborne and Mendel established that for normal growth 18 per cent of the caloric ration should be proteins. They have proved with Ackroyd and Hopkins that these proteins must be rich in lysine and histidine, which are the most important amino acids of growth.

As worked out particularly by the French school, vitamin A is chiefly a vitamin of growth. Vitasterin A is found only in animal aliments. In the form of "prévitamines" (an expression of Lesné and the Richets) it exists in various vegetables. It is to be found in the form of carotenes $\alpha$ and $\beta$ ($C_{40}H_{56}$). The carotenes are transformed in the liver into vitamin A ($C_{20}H_{30}O$); this transformation is often incomplete. Carotene $\beta$ can theoretically divide itself into two molecules of vitamin A; carotene $\alpha$ gives only one molecule. The digestive absorption of carotene is often difficult, because of part of it being retained by cellulose rejected by the bowels. The biologic value of carotenes is less than that of vitamin A.

The vitamin specialist Javillier maintains that a certain quantity of growth vitamin A must always be given in the form of the genuine vitamin A and that the remainder can be pro-

vided as carotenes. For adults the vital or functional minimum of vitamin A (antixerophthalmic and of growth) is admitted to be 0.5 mg. daily, the optimal dose 1.5 mg., of which 0.5 mg. must be given in the form of vitamin A and 1 mg. (corresponding to 2 mg. of carotene) can be taken in the form of carotene. Javillier believes that children need a dose only half as large. Richet, on the contrary, maintains that children must have more vitamin A than adults because there is no growth for adults and because xerophthalmia and hemeralopia are more frequent among adolescents and children than among adults. Frogé has found in 70 children aged 14-18 years in Lille 47 suffering from hemeralopia. All belonged to badly nourished workmen's families. Examining other children from Paris, he found the same proportion.

The problem of vitamin B is more complex. We do not know exactly that vitamin $B_2$, or riboflavin, figures in the growth of a child. This vitamin, as well as vitamins $B_5$, $B_4$ and $B_8$, is clinically and biologically still rather badly individualized. The avitaminosis syndrome of $B_2$ is not known in man. Riboflavin is probably synthesized by vegetables and accumulated in animal tissues. Most aliments contain riboflavin, and it seems that it is contained in a sufficient quantity in the present food of children. Javillier states that the content of vitamin A in certain aliments is as follows (in milligrams and per hundred grams of eatable products the content in carotene and vitamin A):

| Carotene (Exclusively Vegetable Aliments) | | Vitamin A (Exclusively Animal Aliments) | |
|---|---|---|---|
| Spinach | 6 | Liver (veal) | 6 |
| Carrots | 2 | Butter | 2 |
| Pumpkin | 1.2 | Egg yolk | 2 |
| Lettuce | 1.2 | Tunny | 0.30 |
| Watercress | 0.9 | Oysters | 0.12 |
| Tomato | 0.9 | Herring | 0.09 |
| Maize | 0.3 | Cow's milk | 0.09 |
| Peas | 0.1 | Muscles | 0.02 |

Corn germs contain 0.2 to 0.3 mg. of carotene and potatoes about 0.04 mg. per hundred grams of product.

The quantity of genuine vitamin A is absolutely insufficient in the present food ration, which is almost entirely deficient in butter and extremely poor in meat. This is the reason for growth difficulties signalized by all physicians after many examinations of school children.

Professor Hédon, Montpellier physiologist, signalized that examinations performed by him in 1941 revealed a slight deficit of vitamin A in 50 per cent of the children examined. This year the examinations prove that the rate of vitamin A is absolutely insufficient in 80 per cent of the children examined.

### Present Increase of Scabies

At a recent meeting of the Académie de médecine Professor Leroux and Dr. Pignot reported that, in 1941, 60,567 scabies patients were treated in the Hôpital St. Louis in Paris. The annual average from 1920 to 1938 was 4,500-5,000. In comparison with the period before this war the development of scabies has been multiplied at least by 5 and sometimes even by 30. Many persons suffering from scabies believe the restriction of bread to be the cause of this disease, calling it "gale de pain" (scabies due to bread). In nearly all cases it is, however, a genuine human parasitic scabies. This epidemic of scabies is due to two causes: (1) the war, the evacuation of children and the exodus of June 1940; (2) deficient hygiene, which is prolonging and maintaining this epidemic on account of the lack of soap and of individual hygiene. The monthly allowance of soap for hygienic use and also for washing underwear and linen amounts to only 75 Gm. On account of a special law physicians, surgeons, dentists, veterinarians and professional nurses get a supplement of 150 Gm. of soap for their personal use and 500 Gm. of soap detergents for other use.

The treatment of this great number of scabies patients at first involved enormous difficulties because fat and benzyl benzoate are lacking. Lerou reports that, nevertheless, he has succeeded in treating the patients by means of an ointment prepared of sulfur and its compounds; the base was made of a colloid clay of the bentonite series, which has replaced the lacking fatty substances. After soaping the body and after a bath one applies, as soon as the patient comes out of the bath without having wiped himself, this paste in a thin but continuous layer. After twenty-four to forty-eight hours a simple bath is given. The results of this treatment are satisfactory.

Lannay and Verliac explain the scabies epidemic among children in the April issue of *Hôpital*. In infants the disease can manifest itself often in the form of an impetigo or a pyodermitis. Lannay proposes to treat the secondary infection with a sulfonamide applied locally in an ointment and by mouth. With these medicaments he has obtained good results in numerous cases and has been able to proceed quickly with the antiscabies treatment.

### Death of Professors Loir and Marfan

One of the last direct collaborators of Pasteur has died. Professor A. Loir did much research work with him and rendered great service at the period in which Pasteur was affected by hemiplegia. Loir founded the Pasteur institutes of Leningrad, Sidney, Tunis and Rhodesia. For some time he has been professor of biology and pathology at Montreal. He was a corresponding member of the Académie de médecine. An eminent hygienist, he was until lately director of the Bureau d'hygiène of Le Havre.

One of the greatest pediatricians of France, Prof. A. B. Marfan, has died at the age of 83. He was the disciple of Professor Lasègue. In 1912 he was professeur agrégé at the Faculté de médecine of Paris and then professor of hygiene and of the child clinic at the Hôpital des enfants assistés. His first researches were on tuberculosis. He proved that a local attack gives a certain immunity against severe forms of the disease. He studied the secondary syndromes of malignant diphtheria. He described a new disease called dolychostenomelia. Until lately he was president of the Comité national de l'enfance.

## Marriages

RALPH L. BEST, Newport, Ark., to Miss Rachel Ward Browne of Tuscaloosa, Ala., in Tulsa, Okla., in June.

THOMAS HASELL WRIGHT JR., Philadelphia, to Miss Elizabeth Sergeant Odell of Concord, N. C., June 13.

HILIARY H. HENDERSON JR., Greenville, Ala., to Miss Margaret Drennen Bissell of Birmingham in June.

HAROLD FOREST OAKES, Laura, Ill., to Miss Beulah Lynch of El Paso, Texas, in Reno, Nev., May 16.

JEROME CHAMOVITZ, Aliquippa, Pa., to Miss Irma Rae Goldstein of Ambridge at Pittsburgh, June 28.

HOWARD HILT HAMMETT JR., Atlanta, Ga., to Miss Katherine West Johnson in Rome, June 12.

WILLIAM CRAIG PARKS to Miss Mary Ruth Brower, both of High Point, N. C., June 20.

JOSEPH A. CARBONE to Miss Damaris Snell, both of Gary, Ind., in New York recently.

FERDINAND GEORGE KOJIS to Miss Harriet Henderson, both of New York, June 6.

HERBERT CHARLES MAYER to Miss Clara M. Bauer, both of Brooklyn, June 6.

WILLIAM J. STAPLETON JR. to Miss Helen Vernon Hall, both of Detroit, June 20.

JOSEPH L. SPEZIA, Herrin, Ill., to Miss Eileen O'Keefe of Chicago in June.

# Deaths

**Alice Gertrude Bryant** ✠ Boston; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1890; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the New England Otological and Laryngological Society; fellow of the American College of Surgeons; on the staffs of the Vincent Memorial Hospital, the New England Hospital for Women and Children and the New England Deaconess Hospital; aged 80; died, July 25, in the Palmer Memorial Hospital of carcinoma of the cecum and diabetes mellitus.

**Gustav Kolischer** ✠ Chicago, Medizinische Fakultät der Universität Wien, 1886; formerly associate professor of genitourinary diseases, Post-Graduate Medical School; president of the Chicago Gynecological Society in 1910, of the Chicago Urological Society in 1916 and 1932 and of the American Congress of Physical Therapy in 1932; member of the American Urological Association; founder of the departments of genitourinary diseases and member of the staffs of Mount Sinai Hospital and Michael Reese Hospital, where he died, August 11, aged 78, of pneumonia.

**Charles Lemuel Marston,** Mason City, Iowa; Rush Medical College, Chicago, 1893; member of the Iowa State Medical Society; fellow of the American College of Surgeons; past president of the Cerro Gordo County Medical Society; served with the American Expeditionary Forces during World War I; retired lieutenant colonel in the medical reserve corps; formerly member of the House of Representatives; on the staffs of the Story and St. Joseph's Mercy hospitals; aged 72; died, June 25, of coronary thrombosis.

**Dred Rumley Dorente,** Ada, Okla.; College of Physicians and Surgeons, Dallas, Texas, 1907; Chicago College of Medicine and Surgery, 1913; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; specialist certified by the American Board of Otolaryngology; formerly on the staffs of the Sparks Memorial Hospital and St. Edward's Mercy Hospital, Fort Smith, Ark.; aged 61; died, June 17, of cerebral hemorrhage and hypertension.

**George Moses Price** ✠ New York; University of the City of New York Medical Department, New York, 1895; inspector for the health department from 1895 to 1904; director of the joint board of sanitary control; medical director of the Union Health Center; author of "A Handbook on Sanitation," "Tenement Inspection," "Hygiene and Public Health," "Hygiene and Sanitation for Nurses" and "The Modern Factory"; aged 78; died, July 30, of cerebral thrombosis and general arteriosclerosis.

**Clarke Campbell Patton** ✠ Ashland, Ohio; University of Wooster Medical Department, Cleveland, 1910; past president of the Ashland County Medical Society; served as a first lieutenant in the medical corps of the U. S. Army at base hospitals in France during World War I; formerly assistant pathologist and bacteriologist at the University of South Dakota, Vermillion; on the staff of the Samaritan Hospital; aged 58; died, June 11, of coronary disease and diabetes mellitus.

**Jesse Luther Lenker** ✠ Harrisburg, Pa.; Baltimore Medical College, 1907; past president of the Pennsylvania Heart Association; past president and secretary of the Harrisburg Academy of Medicine and the Dauphin County Medical Society; fellow of the American College of Physicians; served during World War I; for many years president of the staff and formerly medical director of the Harrisburg Hospital; aged 59; died, June 2, of cerebral hemorrhage.

**Kyle Bear Steele** ✠ New York; University of Virginia Department of Medicine, Charlottesville, 1913; associate professor of clinical obstetrics and gynecology at the Cornell University Medical College; fellow of the American College of Surgeons; served during World War I; on the staffs of the Booth Memorial Hospital, New York Hospital and the New York Infirmary for Women and Children; aged 52; died, June 18, of coronary heart disease.

**Stanley G. Miner** ✠ Detroit; Detroit Medical College, 1882; emeritus professor of otology, laryngology, rhinology and physical diagnosis at the Wayne University College of Medicine; member of the American Academy of Ophthalmology and Otolaryngology; member of the city public welfare commission from 1913 to 1919; for many years on the staff of St. Mary's Hospital; aged 81; died, June 28, of chronic myocarditis.

**Benjamin Alonza Rice,** Forest, Va.; Medical College of Virginia, Richmond, 1904; member of the Medical Society of Virginia; served as a captain during World War I and was associated with the surgeon general's office in Washington; formerly on the staff of the U. S. Veterans' Hospital, New Haven, Conn.; aged 63; died, June 16, in the Virginia Baptist Hospital, Lynchburg, of coronary thrombosis.

**Isaac Morris Heller** ✠ New York; Yale University School of Medicine, New Haven, Conn., 1896; specialist certified by the American Board of Otolaryngology; member of the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; member of the medical board and on the staff of the Lebanon Hospital; aged 70; died, June 7, of coronary occlusion.

**Earle Carlisle Willoughby** ✠ North Reading, Mass.; Tufts College Medical School, Boston, 1911; member of the New England Society of Psychiatry and the New England Roentgen Ray Society; on the staff of the North Reading State Sanatorium; formerly on the staff of the Tewksbury State Hospital and Infirmary, Tewksbury; aged 60; died, June 23, of cerebral hemorrhage.

**Thomas Oliver Williams,** Tunkhannock, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1906; member of the Medical Society of the State of Pennsylvania; served in the Spanish-American War and World War I; county medical director; chairman of the Wyoming County Selective Service System; aged 61; died, June 14, of coronary occlusion.

**John Edward McHale,** Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1931; member of the Medical Society of the State of New York; aged 36; on the staffs of the St. Catherine's Hospital, Evangelical Deaconess Hospital, Kings County Hospital and the Victory Memorial Hospital, where he died, June 22, of malignancy of the lung.

**Vernon Greene Clark** ✠ San Diego, Calif.; Missouri Medical College, St. Louis, 1896; past president of the San Diego County Medical Society; served in the U. S. Navy during World War I; fellow of the American College of Surgeons; assistant superintendent of the San Diego County General Hospital; aged 69; died, June 6, of coronary heart disease.

**Edward Albert Cunningham,** Belmont, Mass. (licensed in Massachusetts in 1904); served as a captain in the medical corps of the U. S. Army during World War I; aged 61; on the staffs of the Cambridge Hospital, Waltham Hospital, St. Elizabeth's Hospital, Boston, and the Soldiers' Home Hospital, Chelsea, where he died, June 14, of hypertensive heart disease.

**Howard Leon Jameson** ✠ Philadelphia; Medico-Chirurgical College of Philadelphia, 1906; professor of clinical medicine at the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; aged 61; died, July 1, of cerebral thrombosis.

**George Forbes** ✠ Brooklyn; University of the City of New York Medical Department, New York, 1890; fellow of the American College of Physicians; member of the Radiological Society of North America, Inc.; attending roentgenologist to the Wyckoff Heights and Bethany Deaconess hospitals; aged 74; died, June 23, of carcinoma of the colon.

**William Sylvester Darling,** Milwaukee; Wisconsin College of Physicians and Surgeons, Milwaukee, 1903; member of the State Medical Society of Wisconsin; served in the medical corps of the U. S. Army during World War I; on the staff of St. Joseph's Hospital; aged 65; died, June 16, of cerebral hemorrhage, pneumonia and bronchiectasis.

**Robert Stockton Hinchman,** McKeesport, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1906; member of the Medical Society of the State of Pennsylvania; served in the medical corps of the U. S. Army during World War I; on the staff of the McKeesport Hospital; aged 61; died, June 23, of carcinoma of the stomach and liver.

**Adah McMahan** ✠ LaFayette, Ind.; Northwestern Woman's Medical School, Chicago, 1897; served in France during World War I; formerly member of the state board of health; aged 73; on the staffs of the LaFayette Home Hospital and St. Elizabeth Hospital, where she died, June 24, of postoperative shock following cholecystectomy.

# Bureau of Investigation

## STIPULATIONS

### Agreements Between Federal Trade Commission and Promoters of Various Products

The following items are abstracts of stipulations in which promoters of "patent medicines," or medical devices have agreed with the Federal Trade Commission to discontinue certain misrepresentations in their advertising. These stipulations differ from the "Cease and Desist Orders" of the Commission in that such orders definitely direct the discontinuance of misrepresentations. The abstracts that follow are presented primarily to illustrate the effects of the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act on the promotion of such products.

**Amogen Tablets.**—In July 1941 J. R. Hodges, trading as Amogen Company, San Antonio, Texas, stipulated with the Federal Trade Commission to cease representing that this product, a laxative, gets the poison out of the system, causes the bile to flow, effectively treats biliousness, malaria, common colds and fever, poor digestion, acid or gas on the stomach, the results of excessive eating and drinking, headaches, neuralgia, rheumatism and some other disorders or that the tablets will enable one to maintain health and avoid sickness. Hodges further stipulated that he would discontinue any advertisements which failed to reveal that his product contains a mercury derivative which might injure health if taken over a long period of time and that it should not be used when abdominal pain, nausea or other symptoms of appendicitis are present, unless the label itself bears the foregoing warnings. Back in December 1930 the government had declared that the Amogen label and accompanying circular fraudulently represented these tablets as a remedy for indigestion, kidney and liver troubles and some other conditions. At that time the government chemists reported that the tablets consisted essentially of calomel and extracts of plant drugs.

**Bi-Tone Liver Pills and Bi-Tone Wonder Tonic.**—In July 1941 the Bi-Tone Corporation, Bluefield, W. Va., stipulated with the Federal Trade Commission that it would drop the word "liver" as part of the brand name of its pills and cease representing that they have a beneficial effect on the liver; that the "Wonder Tonic" increases vitality or resistance to disease, and that the two products taken together correct ailments originating in the liver, cause the liver to become active and healthy or correct any condition of sluggishness or debility.

**Bragg's Grass Tablets.**—This product is put out under the trade style Live Food Products Company, Burbank, Calif., by a Paul C. Bragg who has posed as a health specialist, food expert and some other things. Bragg represented that the preparation is rich in vitamin A, will prevent sickness, promote health and stimulate activity. In October 1941 the Federal Trade Commission accepted a stipulation from him in which he agreed that he would discontinue these misrepresentations and also cease implying in his advertising that his product has any dietary value other than as a supplemental source of vitamin A to the extent of the number of International Units that it contains.

**Children's Mind Training Program.**—This is a "course" promoted by one E. M. Kellogg of Portland, Ore., who uses the trade style Children's Mind Training Institute. In October 1941 the Federal Trade Commission announced that Kellogg had stipulated that he would cease using the word "Institute" as part of his trade name or otherwise representing that his business is an institution or organization of learning with a staff of competent, experienced and qualified educators.

**Colonial Bread.**—That this is "not fattening," is necessary in a reducing diet, helps burn up body fat, enables one to reduce safely or that six slices of the bread in a reducing diet will give one energy and prevent fatigue or nervous strain or that the bread will protect the user from the harmful residues that cause fatigue or that it protects one's health while reducing, are misrepresentations which the Colonial Baking Company, St. Louis, agreed to discontinue, in a stipulation that it signed in August 1941 with the Federal Trade Commission.

**Dobbs Truss.**—This was represented by the Dobbs Truss Company, Birmingham, Ala., as a device helpful in the treatment of rupture and the first major advancement in truss designing wholly different from any other. It was alleged to hold any rupture, to be a natural healer that would aid nature in curing a rupture and bring muscles together in a manner that would cause or enable them to adhere. In October 1941 the Dobbs concern signed a stipulation with the Federal Trade Commission, agreeing to discontinue these misrepresentations.

**Eureka Springs Ozarka Water.**—In August 1941 Richard R. Thompson, trading as Eureka Springs Water Company and as Ozarka Water Company, Eureka Springs, Ark., stipulated with the Federal Trade Commission that he would discontinue the following misrepresentations in the sale of this product: that it is a cure or competent treatment for any disease; that it is a laxative or that faulty elimination is the cause of all stomach trouble, indigestion, rheumatism or diseases of the liver, kidneys or bladder; that this water has any value due to radioactivity; that it is the purest natural water on the American continent or known to scientists; that undistilled or naturally pure water is the only water to be recommended for use or that distilled water is poisonous.

**Hercules Wild Juices.**—Under the Hercules brand the Food Balance Corporation of Chicago puts out four juices purporting to be based on wild fruits. In August 1941 this concern stipulated with the Federal Trade Commission that it would no longer represent that its "Hercules Wild Blackberry Juice" will prevent or benefit anemia or favorably affect such symptoms of it as fatigue, palpitation of the heart, pains in the head or the back or lack of sex vigor, or offer any material benefit during menstrual periods; that "Hercules Wild Cherry Juice" will serve as a general tonic or invigorate the system or beneficially affect the heart or bowel muscles, stomach walls, liver, uterus or other parts of the body; that "Hercules Wild Blueberry Juice" will tone or otherwise benefit the system or prove an effective antacid or stomach remedy; that "Hercules Wild Elderberry Juice" will have an invigorating or curative effect on the female generative system or that any of these juices will purify the blood, will overcome disorders of the body or be of significant nutritional or medicinal value or supply minerals or other elements in significant amounts.

**Home Treatment Products.**—These are put out by a James M. O'dell, trading as The Home Treatment Service, Chicago. They consisted of "Pur-Erb Compound No. 1," "Laxative Tea Compound," "Bathing Tea #22," "Fu-Tina," "Nerve Sedative Compound" and "Home Ointment." In August 1941 O'dell stipulated with the Federal Trade Commission that he would cease representing that the use of one or more of these products is a cure or remedy for physical disorders, or that through such use health may be regained, the body, nerves or blood strengthened, cleansed or healed or operations avoided; that such use is an effective treatment for stomach disorders, eyestrain, rheumatism, intestinal and kidney troubles and some other conditions. O'dell further agreed to cease representing that Pur-Erb Compound No. 1 is a remedy for stomach ailments; that Nerve Sedative Compound will make the nervous system healthy or that Home Ointment is an effective treatment for rheumatism, neuralgia or similar disorders; that anything he designated by the term "Pur-Erb" or similar term is composed entirely of herbs, unless such is the fact, or, through his use of the words "Nerve Sedative" or any similar terminology, that any product of his possesses sedative properties.

**Lacto-Cal.**—This is put out by one Olive M. Goulet, trading as the Lacto-Cal Laboratories, Los Angeles, who stipulated with the Federal Trade Commission in August 1941 that she would withdraw the following misrepresentations in the sale of her product: that it benefits the nerves, speeds up or aids digestion or increases the flow of the gastric juices; that it possesses tonic effects and is a general gland builder; that it will feed the brain, nerves, tissues, testicles or ovaries; that the preparation is a scientific compound of lactic acid and calcium or contains calcium in sufficient amounts to be of therapeutic value; that its use will reduce acidity or afford relief for that condition or be of benefit to the circulatory system or affect the metabolism; that it will prolong life or enable one to live to be 100 years old or any other definite age; that it contains vitamin B, vitamin D, phosphorus or any elements essential to the building of hemoglobin, or that the general dietary condition of the American people is such as to make the use of Lacto-Cal advisable. It is worth noting also that in February 1938 a district federal court declared that a consignment of Lacto-Cal that had been shipped in interstate commerce was fraudulently represented on the labels as a cure for rheumatic conditions, intestinal disorders, heart trouble and many other things. Government chemists reported that it was essentially a mixture of water, lactic acid, calcium lactate and small amounts of compounds of sodium, magnesium, chlorine and sulfur, as well as volatile acid and coloring.

**LD-Lax and Lacto-Dextrin.**—These are products of the Battle Creek Food Company, Battle Creek, Mich., which in October 1941 signed a stipulation with the Federal Trade Commission to discontinue the following misrepresentations: that LD-Lax relaxes or rests the colon or intestines, combats or allays infection in the colon, is a remedy or cure for constipation and has value as a treatment for stomach disorders, and that Lacto-Dextrin restores health to the digestive system and a healthy balance to the intestines, besides dispelling headaches, nervousness, exhaustion, morning fatigue, gastric acidity and some other ailments.

**Natural Health Products Nostrums.**—These are put out by a Morris Botwen of New York, doing business as the Natural Health Products Company. In October 1941 the Federal Trade Commission reported that Botwen had signed a stipulation in which he agreed to discontinue advertising misrepresentations of which the following are brief abstracts: that "Vitameal" is a "life food" loaded with minerals and vitamins; that "Instant Manam" is a cure or remedy for intestinal disorders and other diseases; that "Vita-Ferro" is a soybean milk drink rich in iron, phosphorus or other organic materials; that "Co-Veg" is a substitute for coffee, antidotes its effects and is rich in any vitamin or mineral; that "I-O-Sol" will prevent or overcome pyorrhea or other mouth diseases; that "Sea Tabs" is a gland tonic; that "Natural Herb Tea" is a cure for skin eruptions; that "Vegeton Soap" corrects enlarged pores or prevents athlete's foot or other skin infections; that "Vegeton Hair Preparation" is of value in treating dandruff, brittle or falling hair; that "Vegeton Skin Cream" is antiseptic and keeps the skin youthful; that "Tupelo Honey" is a remedy for asthma; that "Garlic and Parsley Pellets" is valuable in treating high blood pressure or that "Natural Herb Tea," "Euca Pine Oil" and "Vegeton Body Soap" when used alone or in combination give relief in rheumatism, arthritis or neuritis. Botwen further agreed to cease using the term "Vita" as part of the brand name for any of his products or otherwise implying that they contain vitamins in significant amounts; to discontinue using the term "Ferro" as part of the brand name for Vita-Ferro and representing that it contains iron in significant amounts. He further agreed to drop the term "Instant" in Instant Manam which would imply that it has immediate action, and also the term "Veg" as part of the brand name of Co-Veg, or otherwise to cease representing that it is composed wholly of vegetable ingredients.

**Ozone-Air.**—This was put out by a Clyde Scherpness, trading as Ozone Air Company, Grand Rapids, Mich. In September 1941 Scherpness stipulated with the Federal Trade Commission that he would discontinue advertising that his machine or devices designated "Ozone-Air," or any similar devices, have any therapeutic value; that they will eliminate foul air or offensive odors, oxidize all foreign matter in the air, destroy everything not naturally a component part of the air or render carbon monoxide harmless, or that they are conducive to health.

**Phillipps and Vigro Products.**—These were put out by a Stanley N. Phillipps and a Walter M. Grome, doing business as Parks-Phillipps Health Foods Company, formerly Parks Health Food Company, Cincinnati. In September 1941 these persons stipulated with the Federal Trade Commission to discontinue the following misrepresentations in their advertising: that "Phillipps Alfalfa and Mint Tea" is of any benefit in treating prostatic trouble, overacidity, arthritis and rheumatism; that "Phillipps Wheat Germ Meal" is rich in four vitamins, revitalizes and restores needed elements to the diet, benefits faulty digestion and nervous conditions except those caused by a vitamin B deficiency; that "Phillipps Vegetable Muceen" is of any appreciable value in treating stomach ulcers, hyperacidity or colon irritation; that "Vigro Garlic Tablets" are rich in vitamins A, B and C or in potassium, calcium, phosphorus, iodine or food chemicals or possess any nutritional value or produce any appreciable therapeutic effect beyond that of a slight temporary decrease in blood pressure; that "Vigro Vitamin Tablets" help to combat germs, eradicate colds or furnish an abundance of protection against every possible winter sickness or that "Vigro Laxative No. 2" increases intestinal or liver activity.

**Right-O Products.**—In September 1941 Robert M. Frochlich, trading as Right-O Products Company, New York, stipulated with the Federal Trade Commission that he would withdraw the following misrepresentations in the sale of his preparations: that "Rejuvene" restores physical and mental freshness, removes symptoms of fatigue or the feeling of old age and improves the texture of the skin and tissues; that "Ureduce" supplies certain mineral salts needed for normal gland function or takes off excess weight or fat without exercise, dieting, use of equipment or loss of time; that "Testitotal" has a maximal content of hormones, benefits cases of functional sexual incompetency in men or enhances vital energies; that "Sengovan" is made in Germany, prepared according to latest "scientific experiences" and gives marvelous or immediate results in all cases of sterility; that "Okasa" is a specific against impotence and has been tested or recommended by professors and physicians; that "Oototal" helps to preserve nervous vigor in women or increases vital activities and that "Neuramag" is a prophylactic during influenza epidemics. Frochlich also agreed to cease representing that his products are tested and standardized by the most recent physiological and chemical methods and that he maintains or operates a laboratory unless such statement is true. Further, he agreed not to publish in connection with his name the word "Doctor" or "Dr." unless it is explained that he is not a doctor or practitioner of medicine.

**Ringo.**—That this product can be relied on to cure stubborn cases of ringworm and athlete's foot and be a remedy for psoriasis, soft corns, poison ivy, eczema and skin diseases in general were misrepresentations which Goldie V. Fowlkes, trading as the Ringo Company, Detroit, agreed to eliminate from her advertising, in a stipulation which she signed with the Federal Trade Commission in November 1941.

**Rubel's High Vitamin $B_1$ Wheat Bread.**—This is also sold simply as "Rubel's High Vitamin Wheat Bread." Frederic W. Ziv, Inc., Cincinnati, an advertising agency, signed a stipulation with the Federal Trade Commission in August 1941, agreeing to cease disseminating advertisements for the Rubel Baking Company, Cincinnati, in which certain misrepresentations were made for the Rubel product. Among these were that the bread contains per loaf as many as 800 International Units of Vitamin $B_1$ or more of that vitamin or any other than is actually the case, or that when eaten in quantities ordinarily consumed, the bread will supply the minimum daily nutritional requirement for vitamin $B_1$.

**Snare's Re-Lef.**—A stipulation regarding this product was signed with the Federal Trade Commission in August 1941 by Henry I. Snare, trading as Snare Brothers Ointment Company, and George J. Mergenthal and George O. Dennis, trading as Snare's Re-Lef Sales Company, all of Chillicothe, Mo. In this they agreed to cease representing that the use of their product will prevent or cure pneumonia, asthma, hay fever, influenza, pleurisy, gout or goiter; furnish any appreciable relief from sinus disorders or various forms of rheumatism, prove beneficial in the treatment of appendicitis or severe chest colds and all types of inflammation or kill infection and germs by vapor action; that their preparation is a modern or new type of treatment and superior to similar preparations, has any properties aside from those of a counterirritant or offers more than temporary, local relief to persons suffering from minor bruises or aches. Incidentally, in December 1939, Henry I. Snare pleaded guilty in a district federal court in Missouri to the charge of shipping a consignment of Snare's Re-Lef under fraudulent representations that the product was a remedy or cure for pneumonia, rheumatism, appendicitis and some other disorders and was fined $25. Government chemists reported at that time that Snare's Re-Lef was essentially a mixture of volatile oils including mustard, wintergreen, menthol and a camphoraceous oil in a petrolatum base.

**Tonico Del Cappuccino.**—That this has been approved by legal authorities, is a general tonic, possesses any other than bitter tonic properties, will increase weight, is indispensable for children or has any value beyond that of a stimulant to the appetite, were claims to be discontinued in the advertising, as stipulated with the Federal Trade Commission in August 1941 by Salus Laboratory, Inc., trading as Italian Imperial Company, Brooklyn.

**Tummy Toner.**—This is put out by a Max H. Newman, trading as the Tummy Toner Company, New York. In December 1941 he stipulated with the Federal Trade Commission that he would discontinue the following misrepresentations: that the product will promote nutrition, aid digestion, sustain health or provide a short cut to better health, will help build one up, or curb his appetite for rich, fattening foods; that it will make milk more digestible or double its nutritional value or that Tummy Toner is rich in vitamin B or will give one added energy. Newman further agreed to cease representing by use of the designation "Tummy Toner" as a brand name, or any other expression, that his product will tone the stomach or have any value in respect thereto.

**Van-Tox.**—This alleged treatment for the liquor habit is promoted by one Harry J. Knorr, trading as Laboratory Products Company, Glendale, Calif. It consists of two kinds of tablets containing the same active ingredients, but in different quantities, and these are described as "Special Formula Single Stg. $1" and "$2." In September 1941 Knorr stipulated with the Federal Trade Commission that he would cease representing that "Van-Tox" or any similar preparation is a cure, remedy or effective treatment for chronic alcoholism or that its use will overcome the craving for alcohol and is in all cases harmless. Knorr also promised to cease using the word "Laboratory" or any term of similar meaning in his trade name, or representing in any way that he owns or operates a laboratory.

**Vimm and Palm-Co Products.**—These were put out by Biofoods Corporation of New York City, which in September 1941 signed a stipulation with the Federal Trade Commission to discontinue the following misrepresentations: that "Fortified Palm-Co" is "the modern calcium phosphorus vitamin 'D' aid," or has a beneficial effect on symptoms of nervousness, low resistance, soft teeth, brittle nails and poor endurance, unless these conditions are due to a lack of calcium and phosphorus in the diet, associated with a deficiency of vitamin D; that "Vimm's Wheat Germ Oil Vitamin E Capsules" are a concentrated source of vitamin E; that "Vimm's Powdered Wheat Germ" or "Vimm's Whole Wheat Germ" are excellent sources of vitamins $B_2$, $B_1$, $B_5$ and $B_6$, iron, copper, phosphorus, potassium, manganese, magnesium and other valuable minerals, or that "Vimm's Powdered Wheat Germ" is "ideal" for infant feeding and those on a bland diet. As noted in this department of THE JOURNAL Dec. 20, 1941, page 2188, one Mariano Pollina of New York, who for a time operated as Vimm Wheat Germ Products Company and Moderno Company (at the same street address later used by the Biofoods Corporation) had stipulated with the Federal Trade Commission in March 1941 that he would discontinue certain misrepresentations for "Vimm's Wheat Germ Oil Capsules," "Vimm's Whole Wheat Germ," "Fortified Palm-Co" and "Plain Palm-Co." Some of these misrepresentations were similar to those named in the later stipulation signed by the Biofoods Corporation.

**Vita Health Foods.**—These are put out by a Walter Camp and a Werner Orbach, trading as the Vita Health Food Company, American Health Products Company and Eastern Health Food Stores Association, Washington, D. C. In August 1941 Camp and Orbach stipulated with the Federal Trade Commission that they would discontinue the following misrepresentations in the sale of their products: that "Almano" furnishes complete proteins and other elements found in the main dish of a meal and so may be used interchangeably with other protein foods and is many times as nourishing as beefsteak, eggs, codfish and whole milk, and less expensive; that "Bro-Sak" improves the health of diabetics when substituted for sugar or saccharine and benefits acid stomach and other ailments due to hyperacidity; that "Cali-Kelp Tablets" correct indigestion, skin troubles, rheumatism, obesity, anemia and underweight; that "C-Veg-Salt" is a valuable food accessory or will keep the body alkaline; that a beverage prepared from "Dalmatian Sage Leaves" has a quieting effect on the entire nervous system and benefits colds and kindred ailments; that "Nutrolac" checks harmful intestinal bacteria or helps "stomach sufferers"; that a tea prepared from "O-Pep-O-Mint" is an effective treatment for colds or valuable because of the potassium and manganese that it contains; that "Pomona Grape Juice" will give relief from bad breath, sour stomach or similar ailments; and that "Seven Herbs Laxative" is "fat-reducing," improves kidney function or pancreas action or is recommended by physicians all over the world. Camp and Orbach further agreed to discontinue any advertisements which represent that Cali-Kelp Tablets are always harmless or which fail to reveal that they should not be used by those suffering from lung diseases, chronic cough, goiter or thyroid diseases, except on the advice of a physician and that their use should be discontinued if a skin rash appears. Further, the promoters were to cease running any advertisements of Seven Herbs Laxative which represent this product as being always safe to use or which fail to reveal that its use is potentially dangerous in cases of abdominal pain, nausea, vomiting or other symptoms of appendicitis. This stipulation provided, however, that the foregoing warnings might be omitted from the advertising if the latter cautioned the customer to follow directions on the label, provided that the label did contain the warnings mentioned.

**Vita-Lite.**—According to a stipulation which Vita-Lite, Inc., Portland, Ore., signed with the Federal Trade Commission in September 1941, this concern is to cease representing that its devices or machines designated "Vita-Lite," or any other ozone-generating device of similar character has any therapeutic value or will destroy bacteria or aid in curing disease or that their use is indicated as a remedy or effective treatment for any ailment of the human body. The concern also promised to cease publishing or otherwise disseminating any testimonials containing statements contrary to the terms of the stipulation.

**Vit-O-Net.**—In July 1941 the Federal Trade Commission reported that Vit-O-Net, Inc., Chicago, had signed a stipulation promising to cease representing that this device, an electrical blanket, is a cure for nephritis or obesity or an effective treatment for rheumatism, dropsical conditions, infections, high blood pressure and Addison's disease.

# Correspondence

## CAT ASSAY FOR DIGITALIS PREPARATIONS

*To the Editor:*—The Revision Committee of the U. S. P. XII has adopted a cat assay for the various digitalis preparations. It is to be hoped that this action will not be construed as an endorsement of the clinical practice of transcribing dosage quantities of these preparations into terms of so-called cat units. In previous communications to THE JOURNAL (April 14, 1934, p. 1247) both C. W. Edmunds and H. A. McGuigan protested against this practice and advised that the cat should be left in the laboratory. That their protest was unconvincing seems apparent from the general literature and was voiced by Dr. Robert L. Levy in the answer to their communications. Since the current action of The U. S. Pharmacopeia might be interpreted by some as a vindication of this usage of "cat units" in clinical parlance, it seems appropriate to recall and reemphasize the reasons why such terminology is unwise and even potentially dangerous. The risk which such usage entails comes from the inadvertent support which it affords to the notion that all cardiotonic drugs which are assayed on cats, and for which "cat units" can therefore be computed, can be reduced to a single common denominator of therapeutic potency in terms of their "cat unit" equivalence. That a given number of "cat units" of one preparation does not necessarily have the same therapeutic potency as the same number of "cat units" of a different preparation is testified to by an abundant literature and can be confirmed by any one who consults the suggested dosages for the digitalis and digitalis-like principles and preparations in the current edition of New and Nonofficial Remedies. For example, the average oral daily dose of Tablets Digilanid is equivalent to 2 to 4 "cat units," of Tablets Digalen-Roche to 1½ to 3 "cat units" and of Tablets Gitalen to ⅓ to 1 "cat unit." Obviously their cat unitage does not provide a common measuring stick on which to determine their therapeutic employment or interchangeability. It is equally obvious that disquieting effects might ensue if one substituted say 3 "cat units" of Gitalen in treating a patient who was being maintained on 3 "cat units" of Digilanid or Digalen. Perusal of the clinical literature persuades one that such discrepancies, while widely recognized, are not understood, are confusing and are often interpreted as evidence of the frailties of the assayists and their assays.

The explanation of the necessary discrepancy between such units of biologic activity and therapeutic potency when dealing with unidentical agents can be simplified most readily by analogy. If both epinephrine and ephedrine were assayed as to their biologic activity by intravenous injection in dogs and their activities stated in terms of "pressor units," 10 "pressor units" of epinephrine given by mouth to a patient would not be the therapeutic equivalent of 10 "pressor units" of ephedrine, since the latter is readily absorbed while the former is not. If a long acting barbiturate (e. g. barbital) and a short acting barbiturate (e. g. pentothal) were assayed as to their biologic activity in animals and their activities stated in terms of "hypnosis units," while 10 "hypnosis units" of either might be equally effective and possibly interchangeable for the purpose of inducing sleep in a patient on a single occasion, they would have quite different effects if these doses were administered three or four times daily for purposes of maintaining sedation. In one instance a cumulative effect would be apparent, in the other probably not.

Although there are other ways in which the various cardiotonic glucosides differ from one another, these two differences (absorbability and duration of action) are most significant in determining how they should be used for either rapid digitalization or maintenance. A method of biologic assay cannot dispel these differences. The purpose of the biologic assay is to assure uniformity in potency from sample to sample of the same kind of a digitalis preparation and is not and cannot be a method of equilibrating different kinds of cardiac principles. These remarks are thus not a reflection on the cat method of assay, for it has been proved to be highly accurate and reliable for its proper purpose. Even if facilities permitted a human assay, the "man units" of one preparation would not necessarily be interchangeably equivalent with the "man units" of another. For example, if the "man units" should be defined as that amount of digitalis-like preparation required to "digitalize" an average adult with auricular fibrillation, it would probably require daily doses of about 1/10 to 1/15 "man unit" of digitoxin to maintain such digitalization, while it would probably require daily doses of ¼ to 1 "man unit" of strophanthin for the same purpose, since the former is disposed of slowly and cumulates, while the latter is disposed of much more rapidly.

Therefore, since transcribing therapeutic doses of the digitalis group of drugs into so-called cat units does not serve a useful purpose, increases the confusion of the unwise and may lead to a therapeutic misadventure for the unwary, it should be discouraged.

CARL A. DRAGSTEDT, M.D.,
Northwestern University Medical School,
Chicago.

## ADAMANTINOMA OF THE TIBIA

*To the Editor:*—Drs. Malcolm B. Dockerty and Henry W. Meyerding have presented a valuable study of adamantinoma of the tibia in THE JOURNAL (July 18, p. 932). I have been greatly interested in these apparent enamel organ tumors of the tibia and have had the opportunity of studying sections from the tumor reported by Bishop (*South. M. J.* **30**:571 [June] 1937). They appear to ape the enamel organ tumor but never seem as well differentiated as those occurring in the jaws. It is possible that those in the tibia are merely squamous cell carcinomas resembling the enamel organ tissues by some odd coincidence. It is even possible that the publication of Fischer's case in 1913 attracted attention to this oddity and led to the reports on the 16 subsequent cases between 1930 and 1941. Why should an enamel organ neoplasm select the tibia as its only site remote from the mouth and the orally derived pituitary tissue?

The authors say "We do not feel the necessity of postulating for the mandibular, maxillary, pituitary or tibial types the almost mythical occurrence of anatomic epithelial rests."

It is not necessary to postulate these rests in other than tibial regions. The periodontal membranes of the teeth are usually rich in epithelial rests (débris paradentaire of Malassez), which are derived from remnants of the enamel forming apparatus. McCrea (*J. A. Dent. A.* **24**:1133 [July] 1937) found epithelial rests in the periodontal membranes contiguous with 59 per cent of 60 dental granulomas examined in serial section. In the remaining 41 per cent proliferating epithelium was found. This is hardly a mythical occurrence. Similarly in the case of the pituitary, remnants of Rathke's pouch are factual. It is not my contention that these neoplasms of the jaw and pituitary must be derived from epithelial rests but merely to point out the possibility of such an origin.

Dockerty and Meyerding object to the term "ameloblastoma" while admitting that "adamantimona" is a misnomer. It is true that little will be gained by using this more correct term, but perpetuation of misnomers has prevented progress, in many fields. The term "ameloblastoma" is used in Kronfeld's "Histopathology of the Teeth and Surrounding Structures" (ed. 2, Philadelphia, Lea & Febiger, 1939) and by the Registry of Oral and Dental Pathology of the Army Medical Museum.

HAMILTON B. G. ROBINSON, D.D.S., M.S., St. Louis.
Associate Professor of Oral Pathology, Washington University School of Dentistry.

## CONSTITUTIONAL INADEQUACY

*To the Editor:*—Dr. Walter C. Alvarez in his discussion of constitutional inadequacy in THE JOURNAL, July 4, has rendered a distinct service in emphasizing the importance of this problem. It is no exaggeration to state that 30 to 40 per cent of patients who apply for treatment to the general practitioner or the medical consultant fall into the category of the "constitutionally inadequate." Yet if one peruses the medical literature year in and year out it is apparent that the attention paid to them is inadequate. Dr. Alvarez's continued interest in and occupation with this problem and his insistence that we recognize these patients promptly and so save useless time and money and, in many instances, futile surgery is a notable exception to this lack of interest.

However one may agree with him as to the inherent incurability of the disease and the presence of a constitutional weakness of the nervous system, it is my feeling that our therapeutic armamentarium is not necessarily limited to getting these patients to acquiesce in their symptoms, conserve their energies and limit their activities. From out of this great scrap heap of human rejects can be sorted out several groups which respond satisfactorily to medical treatment. A few of these types are listed by Dr. Alvarez.

The most common group is the type of inadequacy in which digestive symptoms are prominent. These symptoms bear a striking resemblance to the complaints termed "chronic gastrointestinal malfunction." Treatment of these patients with large doses of thiamine hydrochloride over sustained periods of time has proved successful in bringing alleviation of these symptoms and a distinct return of well being. My experience with this drug over the past few years serves to corroborate the findings of Borsook and his co-workers, C. L. Hartsock, Morgan and Barry and others.

Inadequate women at the time of the menopause, with pelvic disturbances as mentioned by Dr. Alvarez, make up another considerable segment of this mass of patients. It is these who frequently border on the involutional melancholic stage and in whom migraine is not an unusual concomitant. I have found estrogenic therapy supplemented with thiamine hydrochloride effective in raising the level of well being in these instances.

Dr. Alvarez aptly states that with all the best intentions in the world we are giving these patients a raw deal. These surgical derelicts with repeated hospital admissions who present themselves with four or five incisional scars are mute evidence of the inadequacy of our understanding of the problem. It is only when we are able to clear our medical thinking of the accumulated débris of the years—was glad to read of a surgeon recommending that the operation for abdominal adhesions be relegated to the dark ages of surgery—and apply intelligently the means of treatment at our command that we shall be able to justify the faith these unfortunates place in us.

JACOB LICHSTEIN, M.D., Philadelphia.

## DEATHS AFTER USE OF MERCURIAL DIURETICS

*To the Editor:*—The July 25 issue of THE JOURNAL contains a series of papers which serve to direct attention to the dangers incident to the use of mercurial diuretics. I wish to call attention to a possible source of misunderstanding.

Three of the deaths described in that issue of THE JOURNAL are reported in duplicate; i. e., 3 of the cases described extensively by DeGraff and Nadler are published elsewhere in the same issue by Brown, Friedfeld, Kissin, Modell and Sussman. The reader should therefore count these deaths as three rather than six. This situation arose unfortunately because we were not aware that personal inquiries concerning these cases by DeGraff were to result in a publication.

It is indeed important to point out the dangers of the mercurial diuretics, but it is equally important not to overemphasize these dangers in view of the fact that these drugs constitute one of the most important groups of modern therapeutic agents.

WALTER MODELL, M.D., New York.

## DIABETES MELLITUS AND PYOGENIC SKIN INFECTIONS

*To the Editor:*—The statistical validity of the article by Dr. John R. Williams entitled "Does Diabetes Mellitus Predispose the Patient to the Pyogenic Skin Infections?" published in THE JOURNAL, April 18, seems highly questionable to me. I submitted the entire statistical calculations to the statistician in our Department of Preventive Medicine of New York University College of Medicine. He went over this material, and I am enclosing a copy of his letter to me.

SAMUEL STANDARD, M.D., New York.

*Dear Dr. Standard:*—First, as to association between diabetes and skin infections, the author submits data from four separate sources: namely, two hospitals, one group of patients from four general practitioners and one group of his own patients. For only one of these four groups are the figures complete, and that group directly contradicts his statement: "From these data it is obvious that there is no significant etiologic relationship between pyogenic skin infections and diabetes."

In the first group of 27,209 hospital admissions, 0.64 per cent of the total number admitted were afflicted with boils or carbuncles; 2.42 per cent of the diabetic were so afflicted. The author indicates that he would wish to say that the higher percentage among the diabetic could be attributed merely to normal variations due to chance. In my opinion, however, based on simple statistical rules, if he was to make a study in ten thousand hospital groups similar to this one, he could not expect to find one group showing such a high percentage for diabetic patients due to chance alone. This is considered good evidence that boils and carbuncles will appear more frequently among the diabetic than in the general population. I say this merely to point to the fact that an association between events, based on numbers alone, cannot always be regarded as evidence of a causal relationship.

As regards the second hospital group of 43,980 admissions, there are no figures to indicate what percentage of the diabetic were afflicted with skin infections. I believe that it would be wise for us not to make assumptions regarding the percentage of diabetic patients in this hospital group.

Considering the four groups of patients, only the first three give an indication of the incidence of skin infections in the general population. These are:

| | |
|---|---|
| First hospital group | 0.64 per cent |
| Second hospital group | 0.67 per cent |
| The patients of four practitioners | 4.18 per cent |

On the other hand, among the four groups of patients presented as evidence, only two of them give even a rough indication of the percentage of skin infections among diabetic patients. These are:

| | |
|---|---|
| First hospital group | 2.42 per cent |
| Group of author's own patients, approximately 4 | per cent |

This last figure is again presumptive, because the author states merely that among 500 patients there were thirteen occurrences of boils and seven of carbuncles, and there is nothing to state that there may not have been certain patients with both boils and carbuncles.

Taking the percentages as I have listed them, the 4.18 per cent afflicted among the patients of the four practitioners is a definitely higher figure than for the two hospital groups, and it is of the same order of magnitude as the two figures for diabetic patients. This is the only point in the whole paper which might suggest that the afflictions with skin infections in a general population group could be as great as in a group of diabetic patients. However, on this point there is no evidence that the different groups are comparable, and I would call such an argument weak.

The second point of criticism is that the author's analysis of his 500 patients is not valid. Dr. Williams states that he has seen some of his patients for more than twenty years. On this score he should consider the fact that if he observed a patient for twenty years he was twenty times as likely to observe a skin infection as he would be in a patient observed for only one year. This is the chief reason why his observation of his own 500 patients is in no way comparable with observations on hospital admissions.

A third criticism is the tabulation of the cases which he presents in the article. To begin with, it is irrelevant since the distribution by sex, for example, is not considered anywhere in the article. Moreover, he does not give the number of patients with boils and carbuncles, but, occurrences, which in theory gives no basis for comparison with the other groups discussed. It is unfortunate that the author, although he states that his findings "support the opinions and conclusions of other workers," does not give reference to these "other workers."

H. M. C. LUYKX,
Department of Preventive Medicine,
New York University College of Medicine.

# Medical Examinations and Licensure

## COMING EXAMINATIONS AND MEETINGS

### BOARDS OF MEDICAL EXAMINERS

### BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Aug. 22, page 1445.

### NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part I.* Various centers, Sept. 14-16. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

### EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written. Part I.* Various centers, Feb. 4. Final date for filing application is Nov. 6. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Oral.* Chicago, Dec. 4-5. *Written.* Various centers, Oct. 12. Final date for filing application is Sept. 1. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 19. Final date for filing application is Sept. 1. Asst. Sec., Dr. William A. Werrell, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 13. *Oral. Part II.* May 1943. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral. All Groups.* Chicago, Oct. 8-10. New York, Dec. 13-16. Los Angeles, Jan. 15-16. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and Written.* Chicago, Jan. 9-10. Final date for filing application is Nov. 1. Sec., Dr. Guy A. Caldwell, 3503 Prytania St., New Orleans.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written.* Richmond, Va., Nov. 9-10. Final date for filing application is Sept. 1. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: *Written.* Locally, Sept. 18. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, December. Final date for filing application is Oct. 1. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Chicago, Nov. 27-29. Final date for filing application is Sept. 30. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY. *Part I.* Oct. 7. Final date for filing application is Aug. 22. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY. February 1943 (tentative). Sec., Dr. Gilbert J. Thomas, 1409 Willow St., Minneapolis.

## Illinois April Report

The Illinois Department of Registration and Education reports the written examination (graduates of foreign and Canadian schools given also a practical test) April 7-9, 1942. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Fifty-six candidates were examined, 40 of whom passed and 16 failed. The following schools were represented:

| School — PASSED | Year Grad. | Number Passed |
|---|---|---|
| University of Colorado School of Medicine | (1929) | 1 |
| Chicago Medical School | (1940) | 1 |
| Loyola University School of Medicine | (1941, 2), (1942, 2) | 4 |
| Northwestern University Medical School | (1940), (1941) (1941,* (1942,* 10), (1942)* | 14 |
| Rush Medical College | (1941, 2) | 2 |
| University of Chicago, The School of Medicine | (1940),* (1941)* | 2 |
| University of Illinois College of Medicine | (1941), (1942) | 2 |
| University of Michigan Medical School | (1940) | 1 |
| Cornell University Medical College | (1940) | 1 |
| Woman's Medical College of Pennsylvania | (1940) | 1 |
| Meharry Medical College | (1938) | 1 |
| University of Toronto Faculty of Medicine | (1939) | 1 |
| Medizinische Fakultät der Universität Wien | (1922) | 1 |
| Universita Karlova Fakultat Lékařská, Praha | (1927) | 1 |
| Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin | (1922), (1923) | 2 |
| Universität Leipzig Medizinische Fakultat | (1936) | 1 |
| Regia Università degli Studi di Napoli. Facoltà di Medicina e Chirurgia | (1929) | 1 |
| Regia Università degli Studi di Padova. Facoltà di Medicina e Chirurgia | (1929) | 1 |
| Universität Basel Medizinische Fakultat | (1939, 2) | 2 |

| School — FAILED | Year Grad. | Number Failed |
|---|---|---|
| Howard University College of Medicine | (1926) | 1 |
| Medical College of Ohio | (1901) | 1 |
| Queen's University Faculty of Medicine | (1938) | 1 |
| Medizinische Fakultät der Universität Wien | (1920), (1922), (1923), (1928) | 4 |
| Friedrich-Wilhelms-Universität Medizinische Fakultat, Berlin | (1919), (1939) | 2 |
| Hamburgische Universität Medizinische Fakultät | (1936) | 1 |
| Johann Wolfgang Goethe-Universität Medizinische Fakultat, Frankfurt-am-Main | (1921) | 1 |
| Philipps-Universität Medizinische Fakultat, Marburg | (1923) | 1 |
| Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultat, Bonn | (1923), (1935) | 2 |
| Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau | (1924) | 1 |
| Magyar Királyi Erzsebet Tudományegyetem Orvostudományi, Pecs | (1923) | 1 |

Fourteen physicians were successful in the practical test for reciprocity and endorsement applicants held in Chicago, April 9, 1942. The following schools were represented:

| School — PASSED | Year Grad. | Reciprocity with |
|---|---|---|
| College of Physicians and Surgeons, Keokuk | (1897) | Missouri |
| St. Louis University School of Medicine | (1940)* | Missouri |
| Washington University School of Medicine | (1931)* | Missouri |
| University of Oklahoma School of Medicine | (1938)* | Oklahoma |
| University of Virginia Department of Medicine | (1932)* | Maryland |
| Marquette University School of Medicine | (1932) | Wisconsin |

| School — PASSED | Year Grad. | Endorsement of |
|---|---|---|
| College of Medical Evangelists | (1941) | N. B. M. Ex. |
| Georgetown University School of Medicine | (1939)* | N. B. M. Ex. |
| Northwestern University Medical School | (1941) | N. B. M. Ex. |
| Rush Medical College | (1940) | N. B. M. Ex. |
| Tulane University of Louisiana School of Medicine | (1939)* | N. B. M. Ex. |
| Washington University School of Medicine | (1940) | N. B. M. Ex. |
| Creighton University School of Medicine | (1938) | N. B. M. Ex. |
| Medical College of Virginia | (1935)* | N. B. M. Ex. |

* Licenses have not been issued.

# Bureau of Legal Medicine and Legislation

## MEDICOLEGAL ABSTRACTS

**Malpractice: Alleged Improper Application of Diathermy Treatment.**—The physician defendant in the course of treating an injury to the plaintiff's left hand and arm recommended stated diathermy treatments. Accordingly the defendant Dyer, who was not a physician, applied in the physician's presence a diathermy treatment of the strength and duration prescribed by the physician. Some time later a treatment of the same strength and duration was again given. Apparently painful and permanent injuries resulted. The plaintiff brought suit against both the physician and the layman, charging that there was a joint duty on the part of both of them "to see that said diathermic treatment was properly administered and that the machine was properly operated and that the treatment was suspended and terminated at the proper time so as to prevent injury." It was charged that the defendants failed in this obligation and "carelessly and negligently caused an electrical current of an amperage specified and directed by (the physician) to pass from said machine through plaintiff's said left arm and hand for said period of twenty (20) minutes, although the said (physician) and (diathermist) knew, at the expiration of twenty minutes that the treatment was inflicting severe pain upon the arm and hand of the plaintiff. . . ." The electrical current, the declaration charged, in both treatments was negligently applied under the negligent and careless personal supervision and direction of the physician, and the treatment lasted continuously for twenty minutes notwithstanding the remonstrances on the part of the patient that it was causing her great pain. A demurrer interposed by the physician was sustained and judgment was entered in his favor. The patient then appealed to the Supreme Court of Florida.

Each of the defendants, the physician and the diathermist, acted within a definite sphere, said the Supreme Court. It was the physician's responsibility to advise such treatment as is generally accepted by the profession as the one most likely to cure or relieve the particular injury from which the patient was suffering when she consulted him. It was the duty of the diathermist to apply the heat of a strength and duration designated by the physician. His duty was expertly to follow the instructions given by the physician. There was no claim that the remedy itself, that is the application of electrical current, was improper for one in the patient's condition nor that there was failure on the part of the diathermist to follow the prescription of the physician. Neither was there a charge that the machine was defective. The substance of the allegation is that the intensity of the heat, the duration of the treatment and the

repetition of it constituted negligence resulting in injury. There is in the complaint not only insufficient averment of facts showing negligence but also of facts indicating "unity of design" or "violation of . . . joint duty" owing by both defendants. This is far from showing that there was a joint tortious act on the part of the defendants or concert of action between them, which is necessary to fasten liability on them on the theory that they were joint tort-feasors. The patient contended that the allegations of the declaration abundantly show the characteristics of joint tort-feasorship, citing in support of the contention 2 cases, *Louisville & N. R. Co.* v. *Allen*, 67 Fla. 257, 65 So. 8 and *Feinstone* v. *Allison Hospital, Inc.*, 106 Fla. 302, 143 So. 251, which held that if acts of negligence although distinct in themselves concur in producing an injury the persons guilty of negligence are joint tort-feasors and are jointly and severally liable for the injury. Even granting that rule, however, the court did not believe that it could be applied to the facts in the present case. Even granting, said the court, that the rule is in Florida that when the negligences of two or more persons concur in producing a single, indivisible injury, then such persons as joint tort-feasors are jointly and severally liable, although there was no common duty, common design or concerted action, we still are unable to discern in the pleading allegations which if proved would establish that there was negligence on the part of the physician in his field and on the part of the diathermist in his which concurred in the eventual injury. And the court was not influenced by the charge that the physician was present at the time of the treatment.

The judgment of the lower court in favor of the defendants was accordingly affirmed.—*Hudson v. Weiland, 8 So. (2d) 37 (Fla., 1942).*

**Privileged Communications: Hospital Records; Autopsy Reports; Interns.**—An industrial life insurance policy provided, with certain exceptions not pertinent to the present case, that the insurer assumed no obligation if within two years preceding the date of the policy the insured had been a patient at or an inmate of any institution for the treatment of physical or mental disease, or had undergone any surgical operation, or had been attended by any physician. The policy was issued April 11, 1938. About two months later the insured died in a hospital as the result of "rheumatic heart disease with congestive failure." The insurer denied liability, the trial court directed a verdict for the beneficiary, and the insurer appealed to the United States Court of Appeals for the District of Columbia.

To establish its nonliability, the insurer attempted to prove through a practicing physician that he had treated the insured at weekly intervals during the period between Dec. 25, 1937 and June 6, 1938, the date of her admission to the hospital, and also to prove through the hospital intern the hospital records showing the history, diagnosis and treatment of the insured. An effort was made, too, to introduce in evidence an autopsy report. These records, if admitted, would have shown that at the time of the admittance to the hospital the insured had stated that since 1937 she had experienced shortness of breath and had tired easily; that she had ceased working Jan. 1, 1938 and had then consulted her family physician, who had treated her regularly thereafter; that she had been in bed intermittently since January 1938, and that some years previously she had been treated for syphilis and for rheumatic heart disease and pulmonary tuberculosis. The trial court held this evidence to be inadmissible because of a statute providing that "no physician or surgeon shall be permitted, without the consent of the person afflicted, or of his legal representative, to disclose any information, confidential in its nature, which he shall have acquired in attending a patient in a professional capacity and which was necessary to enable him to act in that capacity." The correctness of this ruling was contested on appeal.

The trial court did not err in excluding the hospital records, in the opinion of the court of appeals. The witness who was offered to prove the records, an intern, stated that the information came from the lips of the patient. The duty of the witness in the hospital required him to obtain the information for the records and for the use of the attending physician. Counsel for the insurance company argued that an intern, not then licensed to practice, was not a physician within the meaning of the privileged communications statute and therefore the information given him by the patient in response to his queries was admissible. The statute is very broad, the court pointed out. It forbids disclosure by the physician of any information obtained by him in his professional capacity. The intern is himself a physician, the court said. He is a graduate of a medical school with a doctor's degree, although he may not be licensed to practice his profession in the ordinary way by so holding himself out to the public. But it is common knowledge that a part of the duty of an intern is to get the medical history of a patient, and in this respect he is the attending physician. Not only this, but in many instances he does the work of a physician and, in other respects, relieves the physician of professional services which he would ordinarily perform. It would be straining the law, the court concluded, to hold that disclosures made to him by a patient are not equally privileged as those made to the physician in charge.

The trial court erred, however, in rejecting the testimony of the other physician who was asked to testify only to the fact that he had been called to attend and had attended and treated the insured in a professional capacity during the two year period immediately preceding the issuance of the policy. This testimony did not relate to any information secured by the physician from the patient but only to facts within his own knowledge and material to the insurance company's case that a fraud had been practiced by the insured in denying to the insurer that she had been previously treated by a physician. Error was committed, too, in rejecting the evidence of the hospital records showing an autopsy on the insured. The competency of evidence of this character, the court pointed out, was decided in *Carmody* v. *Capital Traction Co.*, 43 App. D. C. 245, Ann. Cas. 1916D, 706, in which it was said that the relation between a surgeon performing an autopsy and the body of the dead person is not the relation of physician and patient.

The judgment of the trial court was therefore reversed and the case remanded with instructions to grant a new trial.—*Eureka-Maryland Assur. Co. v. Gray, 121 F. (2d) 104 (1941).*

## *Society Proceedings*

### COMING MEETINGS

American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 11-14. Dr. W. L. Benedict, 102 Second Ave., S.W., Rochester, Minn., Acting Secretary.

American Academy of Physical Medicine, Boston, Oct. 14-17. Dr. Herman A. Osgood, 144 Commonwealth Ave., Boston, Secretary.

American Clinical and Climatological Association, Princeton, N. J., Oct. 12-14. Dr. James Bordley, Johns Hopkins Hospital, Baltimore, Secretary.

American Congress of Physical Therapy, Pittsburgh, Sept. 9-12. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.

American Hospital Association, St. Louis, Oct. 12-16. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Secretary.

American Roentgen Ray Society, Chicago, Sept. 15-18. Dr. H. Dabney Kerr, University Hospitals, Iowa City, Secretary.

Colorado State Medical Society (House of Delegates only), Denver, Sept. 23-24. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver, Executive Secretary.

Delaware, Medical Society of, Dover, Oct. 13-14. Dr. William H. Speer, 917 Washington St., Wilmington, Secretary.

District of Columbia, Medical Society of the, Washington, Sept. 29-Oct. 1. Mr. Theodore Wiprud, 1718 M St. N.W., Washington, Secretary.

Idaho State Medical Association, Sun Valley, Sept. 16-19. Dr. F. B. Jeppesen, 105 North 8th St., Boise, Secretary.

Indiana State Medical Association, French Lick, Sept. 29-Oct. 1. Mr. T. A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.

Kentucky State Medical Association, Louisville, Sept. 27-Oct. 1. Dr. Arthur T. McCormack, 620 South Third St., Louisville, Secretary.

Michigan State Medical Society, Grand Rapids, Sept. 22-25. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing, Secretary.

Mississippi Valley Medical Society, Quincy, Ill., Sept. 30-Oct. 2. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

Nevada State Medical Association, Reno, Sept. 24-26. Dr. Horace J. Brown, 120 North Virginia St., Reno, Secretary.

Oregon State Medical Society (House of Delegates only), Portland, Sept. 12-13. Dr. John R. Montague, 1020 S.W. Taylor St., Portland, Secretary.

Pennsylvania, Medical Society of the State of, Pittsburgh, Oct. 5-8. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.

Vermont State Medical Society, Montpelier, Oct. 1. Dr. Benjamin F. Cook, 154 Bellevue Ave., Rutland, Secretary.

Virginia, Medical Society of, Roanoke, Oct. 5-7. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.

Washington State Medical Association (House of Delegates only), Seattle, Sept. 12-13. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.

Wisconsin, State Medical Society of, Milwaukee, Sept. 14-16. Mr. Charles H. Crownhart, 110 East Main St., Madison, Secretary.

# Current Medical Literature

## AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

### American Journal of Medical Sciences, Philadelphia

**203**:781-928 (June) 1942


*Myocarditis in Poliomyelitis. O. Saphir and S. A. Wile, Chicago.—p. 781.

Age, Sex and Relationships of Auricular Fibrillation. C. F. Garvin, Cleveland.—p. 788.

Coronary Thrombosis in a Young Diabetic. N. Reitman, W. R. Greenwood and J. H. Kler, New Brunswick, N. J.—p. 792.

Brucella Endocarditis with Clinical, Bacteriologic and Pathologic Findings: Case. W. W. Spink, L. A. Titrud and P. Kabler, Minneapolis.—p. 797.

Persistent Tachycardia and Pulse-Temperature Disproportion: Relation to Acute Myocardial Lesions. J. R. Lisa, C. Solomon and D. Eckstein, New York.—p. 801.

*Frequency of Bilateral Renal Disease in Persistent Hypertension. J. R. Kahn and T. C. Laipply, Cleveland.—p. 807.

Renal Concentration Test Employing Posterior Pituitary Extract. W. A. Sodeman and H. T. Engelhardt, New Orleans.—p. 812.

*Preliminary Report on Treatment of Agranulocytosis with Sulfathiazole. W. Dameshek and L. E. Wolfson, Boston.—p. 819.

Abnormal Accumulations of Lymph Follicles in Digestive Tract. P. Gruenwald, Chicago.—p. 823.

Diagnosis of Multiple Myeloma by Sternal Aspiration. L. H. Beizer, B. E. Hall and H. Z. Giffin, Rochester, Minn.—p. 829.

Action of Anti-Pernicious Anemia Principle on Blood Picture of Opossum Pouch-Young and Rat Embryos. J. H. Last and E. E. Hays, Chicago.—p. 836.

Effect of Liver Extracts on Erythropoiesis in Chick Embryo. E. E. Hays, J. H. Last and F. C. Koch, Chicago.—p. 843.

Acetylphenylhydrazine Anemia: II. Bile Pigment Elimination and New Hemoglobin Reconstruction in Bile Fistula Dog. W. O. Cruz, W. B. Hawkins and G. H. Whipple, Rochester, N. Y.—p. 848.

Relation of Pernicious Anemia to Solar Radiation and Skin Cancer. F. L. Apperly, Richmond, Va.—p. 854.

*Treatment of Polycythemia Vera with Lead Compounds. E. H. Falconer, San Francisco.—p. 857.

*Treatment of the Tuberculous Woman During Pregnancy. E. S. Mariette, L. M. Larson and J. C. Litzenberg, Minneapolis.—p. 866.

Systemic Reactions to Mercurial Diuretics. E. M. Kline and W. B. Seymour, Cleveland.—p. 874.

Inefficiency of Immune Globulin in Prophylaxis of Measles During Adolescence. J. R. Gallagher, Andover, Mass.—p. 880.

Effect of Drugs on Circulation in Normal Hands and Feet. H. Montgomery, Philadelphia.—p. 882.


**Myocarditis in Poliomyelitis.**—During the last few years Saphir and Wile encountered 7 patients with poliomyelitis who died during the acute stage of the disease or suddenly (3 patients) several months after the acute process had subsided. At necropsy the hearts of 6 of these patients showed myocardial lesions. The myocardial changes in the 7 patients were characterized by foci of perivascular infiltration of lymphocytes and neutrophils. Monocytes were also present in some instances, and there was a multiplication of adventitial cells. Occasionally inflammatory cells widely invaded the interstitial tissue. Minute foci of lymphocytes were seen just beneath the endocardium. The muscle fibers showed little degeneration. Clinically, the myocarditis was not suspected. The length of time poliomyelitis had existed or its apparent severity had no bearing on the degree of myocarditis found at necropsy. From a review of the patients' clinical records no definite criteria can be laid down for the diagnosis of acute myocarditis in poliomyelitis, since it often runs its course without producing any diagnostic symptoms. Myocarditis should be suspected if the patient suddenly becomes worse and begins to fail rapidly without any apparent reason. Because of the extremely high incidence of myocarditis (6 of 7 patients) its occurrence during poliomyelitis should be borne in mind. Many patients with poliomyelitis, particularly of the bulbar type, die from bronchopneumonia; among the 7, 4 had pneumonia. The perivascular infiltrations were not characteristic of rheumatic myocarditis, and the histories of the patients gave no indication of rheumatic fever. Herzog and Rodriguez, in their discussion of myocarditis in typhus, described among other cells the accumulations of adventitial cells around blood vessels and the rarity of degenerative changes. The changes they described were somewhat similar to those seen in the myocardium of some of the 6 patients with poliomyelitis. Whether or not this indicates that these myocardial changes are characteristic of virus diseases cannot be answered at present, but more careful studies of the myocardium of patients dying from virus disease may determine whether or not virus disease causes a definite, clear and characteristic myocarditis.

**Bilateral Renal Disease in Persistent Hypertension.**—Of 1,000 patients who died of conditions directly related to hypertension and on whom necropsies were performed, Kahn and Laipply point out that all had a final anatomic diagnosis of arterial nephrosclerosis, arteriolar nephrosclerosis or a combination of the two. The renal vascular disease was bilateral in all, but in many the degree of vascular involvement was not the same in the two kidneys. The renal involvement can be so extreme as to produce a functionless or almost a functionless kidney. The weight and size of the kidneys of 456 patients were determined at necropsy, but neither was directly proportionate to the degree or duration of the hypertension.

**Sulfathiazole in Agranulocytosis.**—Dameshek and Wolfson gave sulfathiazole in large doses to 2 patients with agranulocytosis in addition to transfusions and pentnucleotides. The ensuing recoveries of the patients may have been due, in part at least, to the effect of the sulfonamide on the sepsis which was almost certainly present, thus allowing spontaneous leukocytic regeneration in the bone marrow to take place. Sulfonamide drugs may be effective even in the complete absence of granulocytes. It is suggested that a further trial with sulfathiazole or sulfadiazine be made in other cases. When the condition is due to sulfanilamide, the use of sulfathiazole or sulfapyridine and vice versa might be considered.

**Lead Compounds for Polycythemia Vera.**—In the treatment of 11 patients with polycythemia vera Falconer used acetate orally and colloidal lead phosphate intravenously for periods of from one to five years. Nine of them were relatively free from symptoms during treatment and were able to continue their work, but 2 with complicating thrombosis were chronic invalids and were unable to work. Treatment of such patients with lead is contraindicated. Up to the present time no permanent or serious toxic effects have occurred and there have been no deaths. Six of the 11 patients had previously received phenylhydrazine, which they regarded as more toxic and disabling than lead and were unwilling to submit to further treatment with it. Colloidal lead phosphate intravenously in doses of 10 cc. controls the symptoms and reduces the blood level, but it should never be used unless the patient can be kept under careful supervision.

**Treatment of Tuberculous Women During Pregnancy.**—Since September 1921 Mariette and his associates have followed 8 premature deliveries in 8 tuberculous women and 96 full term pregnancies in 86 tuberculous women. They directed their effort to the treatment of the disease process rather than against the normal physiologic process (pregnancy), believing that the tuberculous pregnant woman could go to full term without interfering with her recovery from tuberculosis. Sixty-four of the 86 women were delivered at the sanatorium and 22 elsewhere. Of the 82 followed up, 15 (18.3 per cent) are dead in contrast to 39.1 per cent of all women who were discharged from the sanatorium for the first time during the same period. If those having premature deliveries are considered, 19 (21.6 per cent) are dead in contrast to the 39.1 per cent for all women discharged from the sanatorium for the nineteen years of the study. While the group of tuberculous pregnant women is small, the length of the study gives it some value and seems to indicate that when tuberculosis is properly treated pregnancy probably does not adversely affect the disease. Many variables require further study before it can be explained why the death rate for all women between 18 and 39 years of age

following first discharge is approximately twice that of the pregnant group. Tuberculosis by itself does not necessarily constitute an indication for therapeutic abortion. The modern methods of treating tuberculosis and modern antepartum care apparently offer the tuberculous pregnant woman as good a chance for recovery from the tuberculosis as though pregnancy did not exist. A joint study by sanatoriums holding the same views might yield more conclusive data.

## American J. Obstetrics and Gynecology, St. Louis

**43**:919-1098 (June) 1942. **Partial Index**

*Further Studies on Erythroblastosis Neonatorum of Obstetric Significance. C. T. Javert, New York.—p. 921.

*End Results in Treatment of Carcinoma of Cervix: Fifteen Year Report, 1921-1936. L. C. Scheffey, W. J. Thudium and D. M. Farell, Philadelphia.—p. 941.

Comparative Physiology of Placental Transfer. L. B. Flexner and A. Gellhorn, Baltimore.—p. 965.

Diffuse Luteinization of Ovaries Associated with Masculinization Syndrome. S. H. Geist and J. A. Gaines, New York.—p. 975.

Relationship Between Late Prenatal Hemoglobin Levels and Febrile Puerperal Morbidity. H. J. Bickerstaff, Baltimore.—p. 997.

Abortion in Rabbits Fed Vitamin K Deficient Diet. R. A. Moore, St. Louis; Isabelle Bittenger, New York; Mary L. Miller, St. Louis, and L. M. Hellman, Baltimore.—p. 1007.

Anovulatory Factor in Sterility. L. S. Griffith and W. P. L. McBride, Grand Rapids, Mich.—p. 1012.

Malignancy of Vulva. S. C. Graves and J. Mezer, Boston.—p. 1016.

Intratesticular Hemorrhage: Birth Trauma, with Report of Eight Cases. B. Halpert, New Orleans.—p. 1028.

*Gestation Fourteen Years After Radium Induced Amenorrhea. M. Rosenberg and S. B. Schenck, Brooklyn.—p. 1033.

Evaluation of Particular Mode of Therapy of Trichomonas Vaginalis. C. A. Elden, Rochester, N. Y.—p. 1054.

Treatment of Trichomonas Vaginalis Vaginitis with Negatan (Negatol). W. Filler, N. Drezner and F. H. Adamo, New York.—p. 1057.

Clinical Note on Use of Sulfanilylguanidine in Mycotic Vaginitis. J. L. Pinkston and J. C. Burch, Nashville, Tenn.—p. 1058.

**Erythroblastosis Neonatorum.**—Javert emphasizes certain obstetric features of erythroblastosis neonatorum as revealed by a study of 55 cases. The most prominent clinical feature is the type. Of the 55 cases 17 were hydrops fetalis with a fetal mortality of 100 per cent. The respective figures for the other types were for icterus gravis 27 with 45 per cent mortality, congenital anemia 4 with 25 per cent, hemorrhagic diathesis 4 with 25 per cent and unclassified cases (without the four foregoing features) 3 with 100 per cent mortality. These last 3 infants died in utero and examination disclosed unmistakable evidence of erythroblastosis. The incidence of the disease is 1:438. The fetal mortality rate appears lower among infants born nearer term. Primiparas having such infants seem prone to have subsequent babies with the disease; the recurrence in multiparas is about 50 per cent. This points to a dominant mendelian characteristic inherited from the parents, the Rh factor. An intraplacental hematoma, containing numerous normoblasts and erythroblasts most likely of fetal origin, was found in 8 instances. Such a lesion provides for the transmission of the Rh agglutinogen or some other factor from the fetal circulation to that of the mother. Thus isoimmunization of the mother could take place. The formation of antibodies in the mother and their passage through the placenta into the fetal circulation probably causes erythrocyte hemolysis and the hemosiderin pigment. The chief maternal complications were toxemia of pregnancy and excessive uterine enlargement. Early recognition of the disease in the delivery room, aided by studies of the cord blood, affords an excellent opportunity for prompt treatment. Microscopic studies of the placenta are confirmatory. Damage to the internal organs, particularly the liver, is borne out by pathologic and physiochemical studies.

**Treatment of Carcinoma of Cervix.**—Scheffey and his colleagues saw 293 patients with carcinoma of the cervix between September 1930 and September 1936. Of these they treated 277 and followed up 97.2 per cent. Approximately 7 per cent of the lesions were classified as adenocarcinoma and the others as squamous cell in type. Freedom from signs and symptoms of cervical carcinoma for five years following treatment is in no sense a criterion of "cure." The term "salvage" is used for patients who have survived for five or more years after therapy. The present day or absolute salvage (patients alive following treatment based on total actually seen), the relative salvage (patients alive following treatment based on number actually treated) and the five year salvage (patients treated during the observation period who survived for five or more years but eventually died of carcinoma or an intercurrent condition) are respectively 12.9, 13.7 and 23.1 per cent. Five years ago the respective percentages were 19.2, 20.5 and 25.3. Ten years ago they were 14.2, 15.7 and 20.7. This tends to show that as survivors grow older the mortality rate is influenced by diseases incident to old age and not necessarily due to recurrent carcinoma, unless definitely proved. The percentage of surviving patients more than 40 when they had received their initial treatment is about twice as large as the corresponding percentage of survivors less than 40. Of 5 patients with a group 1 lesion, 2 are alive ten and twenty years, respectively. Eight of 30 patients with a group 2 lesion are alive from five to nineteen years. Of 208 with group 3 lesions 26 are alive from five to nineteen years. None of the 25 patients with group 4 lesions survived the five year period. Of the 19 with group 5 lesions 2 are alive eight and ten years after treatment. Four patients died primarily as a result of treatment. Pelvic peritonitis developed in 2 and the other 2, dying respectively on the eighth and twenty-first postoperative day, exhibited advanced cardiovascular and renal disease in addition to the pelvic changes of advanced carcinoma. Radium therapy was undoubtedly the factor in producing or at least in activating the virulent pelvic infection of the first 2 patients who died.

**Gestation After Induced Amenorrhea.**—A diagnosis of submucous fibroid was made in a woman of 47 who fourteen years ago had a therapeutic radium amenorrhea induced. At operation Rosenberg and Schenck found the uterus smooth and enlarged to about a three months gestation, both ovaries were sclerotic and both tubes were normal. A supracervical hysterectomy and bilateral salpingo-oophorectomy were performed in the usual manner. The pathologic diagnosis was a gravid uterus with placental tissue, and therefore the postoperative diagnosis was incomplete abortion. From the pathologic report (ovaries with evidence of follicular activity and recent corpora lutea) it was deduced that, although no menstruation had occurred, cyclic ovarian function existed. Therefore, owing to some change in the hormone balance the ovaries had regenerated and had again become susceptible to the constant stimulation of the pituitary gonadotropes. This stimulation in time produced a suitable endometrium, so that nidation of the ovum and gestation ensued without previous cyclic bleeding.

## American Journal of Ophthalmology, Cincinnati

**25**:513-642 (May) 1942

Lipemia Retinalis. S. H. McKee, D. R. Wilson, A. F. Fowler and B. Wilen, Montreal, Canada.—p. 513.

Problem of Preventing Partial or Total Loss of Vision in Glaucoma Patients of Eye Clinics: Some Suggestions for Remedial Measures. M. J. Schoenberg, New York.—p. 521.

Familial Degeneration of the Macula Lutea: Review of Literature with Report of Eight Additional Cases. J. W. Crawford, San Francisco. —p. 525.

Use of Riboflavin in Treatment of Corneal Diseases. K. W. Cosgrove and P. L. Day, Little Rock, Ark.—p. 544.

Operation for Congenital Glaucoma. O. Barkan, San Francisco.—p. 552.

History of Orthoptics. M. C. Wheeler, New York.—p. 569.

Visual Prognosis for Aging Lens. R. Von der Heydt, Chicago.—p. 576.

Sterilization of Sharp Instruments by Chemical Solutions: Further Studies. M. H. Post and M. Moor, St. Louis.—p. 579.

Anomalous Retinal Correspondence. D. E. Dicke, Milwaukee.—p. 585.

**25**:643-776 (June) 1942

Ocular Pemphigus and Its Relation to Pemphigus of Skin and Mucous Membranes. J. V. Klauder and A. Cowan, Philadelphia.—p. 643.

Practical Applications of Gonioscopy to Glaucoma Surgery. H. S. Sugar, Vancouver, Wash.—p. 663.

Surgical Removal of Corneal Scars. W. M. James, St. Louis.—p. 672.

Papilledema Without Increased Intracranial Pressure. A. J. Bedell, Albany, N. Y.—p. 685.

Differential Diagnosis of Tropias, with Particular Reference to Value of Orthoptic Training. W. T. Davis, Washington, D. C.—p. 697.

Improved Model of the Kukán Ophthalmodynamometer. A. Linksz, Hanover, N. H.—p. 705.

Sulfanilamide in Treatment of Trachoma: Results After Three Years of Trial. R. Sory, Richmond, Ky.—p. 713.

Cilia Implantation in Anterior Chamber Through Traumatic Corneal Perforation. J. P. Cowen, Chicago.—p. 721.

## American Journal of Physiology, Baltimore

**136**:351-542 (May) 1942. **Partial Index**

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Effect of Body Size on Energy Exchange in Work. S. Robinson, Bloomington, Ind.—p. 363.
Reaction and Neutralizing Ability of Contents of First Part of the Duodenum in Normal Dogs Under Fasting Conditions. J. E. Berk, J. E. Thomas and M. E. Rehfuss, Philadelphia.—p. 369.
Hypothalamic Stimulation Yielding Adrenalin Reversal Effects. M. B. Bender and E. A. Weinstein, New York.—p. 376.
Influence of Benzedrine on Work-Decrement and Patellar Reflex. G. A. Alles and G. A. Feigen, Pasadena, Calif.—p. 392.
Observations on Hemorrhagic Hypotension and Hemorrhagic Shock. J. M. Werle, R. S. Cosby and C. J. Wiggers, Cleveland.—p. 401.
Cardiac and Peripheral Resistance Factors as Determinants of Circulatory Failure in Hemorrhagic Shock. C. J. Wiggers and J. M. Werle, with technical assistance of P. C. Shea, Cleveland.—p. 421.
Study by Quantitative Methods of Spontaneous Variations in Volume of Finger Tip, Toe Tip and Posterosuperior Portion of the Pinna of Resting Normal White Adults. G. E. Burch, A. E. Cohn and C. Neumann, New York.—p. 433.
Disappearance Rate of Tyrosine from Blood of Dogs. J. A. Greene and G. W. Johnston, Iowa City.—p. 460.
Chemical Composition of Human Semen and of Secretions of the Prostate and Seminal Vesicles. C. Huggins, W. W. Scott and J. H. Heinen, Chicago.—p. 467.
Histochemical Changes in Myocardium of Dogs Following Experimental Temporary Coronary Arterial Occlusion. O. H. Lowry, D. R. Gilligan and A. B. Hastings, Boston.—p. 474.
Effect of Sulfanilamide on Ability of Rabbits and Dogs to Withstand High Altitudes. F. L. Lawson, Toronto, Canada.—p. 494.
Measurement of Edema in the Heart-Lung Preparation. E. H. Wood and G. K. Moe, Minneapolis.—p. 506.
Normal Pneumocardiogram. H. A. Blair, A. M. Weld and H. M. Hardwicke, Rochester, N. Y.—p. 523.
Titrations of Human Seminal Fluid with Acids and Alkalis and Their Effects on the Survival of Sperm Motility. L. Shedlovsky, D. Belcher and I. Levenstein, New York.—p. 535.

## American Review of Tuberculosis, New York

**45**:595-782 (June) 1942

Allen Kramer Krause: Brief Biographic Story. H. S. Willis, Northville, Mich.—p. 595.
Allen Krause and the National Association. K. Emerson, New York.—p. 607.
Dynamics of Epidemiology in Relation to Epidemic Tuberculosis. I. Galdston, New York.—p. 609.
War and Tuberculosis. E. R. Long, Philadelphia.—p. 610.
Changing Scenes in Tuberculosis. J. A. Miller, New York.—p. 637.
Immunity in Tuberculosis: Clinical Considerations. F. M. Pottenger, Monrovia, Calif.—p. 651.
Features of Early Pulmonary Infiltration. J. B. Amberson Jr., New York.—p. 660.
Differential Diagnosis in Pulmonary Tuberculosis. J. J. Waring, Denver.—p. 666.
Physical Principles in Pneumothorax. M. Pinner and A. E. Margulis, New York.—p. 676.
Osteoplastic Thoracoplasty. L. Eloesser, San Francisco.—p. 703.
Extrapleural Pneumonolysis with Pack. R. C. Matson, Portland, Ore.—p. 714.
*Pulmonary Coccidioidal Disease. R. A. Peers, Colfax, Calif.; E. F. Holman and C. E. Smith, San Francisco.—p. 723.
*Enlargement of Superficial Lymph Nodes in Brucella Infection. A. L. Bloomfield, San Francisco.—p. 741.
Miliary Diseases of Lungs. C. R. Austrian and W. H. Brown, Baltimore.—p. 751.
Nonpathogenic Acid Fast Bacilli. E. R. Baldwin, Saranac Lake, N. Y.—p. 756.
Chrysotile Asbestos as Indicator of Subtile Differences in Animal Tissues. L. U. Gardner, Saranac Lake, N. Y.—p. 762.

**Pulmonary Coccidioidal Disease.**—Peers and his associates limit their discussion of pulmonary coccidioidal infection to the clinical types in which pulmonary involvement is demonstrable and prominent. The port of entry may be the skin rather than the respiratory tract. Often cutaneous, meningeal, subcutaneous or osseous and articular lesions may develop without clinical or roentgen evidence of a pulmonary lesion. Even at necropsy a coccidioidal focus may be overlooked by any one other than an experienced pathologist on his guard. Many primary coccidioidal infections occur without demonstrable roentgen changes, even though proof through recovery of the fungus from the sputum cannot be challenged. Sometimes clinical symptoms are absent and the proof of infection lies in the change of the reaction to the coccidioidin test. It is extremely difficult to differentiate frank primary pulmonary coccidioidomycosis from tuberculosis on a clinical basis. Usually, as in primary tuberculosis, the infection is focalized. Occasionally a pulmonary cavity develops soon after the primary infection with few symptoms other than an occasional hemoptysis which is not severe enough to endanger life or even health. Dissemination from this lesion is infrequent, even though the fungus may be present in the sputum. Rarely the fungus is not walled off and it disseminates, and then coccidioidal granuloma occurs as an endogenous reinfection. The maximal danger exists relatively soon after the infection is acquired, when every effort should be made to safeguard the patient.

**Lymph Nodes in Brucellosis.**—Recently Wise and Poston reported isolation of Brucella from the lymph nodes of Hodgkin's disease. Bloomfield attempted to ascertain whether in true brucellosis there exists a clinical enlargement of lymph nodes. He had consulted eighty-six papers in English listed in the *Index Medicus* and found 50 cases in which the condition of the lymph nodes was specifically mentioned. Summary of the data reveals that lymph node enlargement is not uncommon. Even if it is assumed that the nodes were not enlarged in all the cases in which no specific mention was made, adenopathy was present in 15.2 per cent; when the state of the nodes was mentioned the percentage was 58. Study of the changes in individual cases, after making allowances for deficiencies of the data, indicates that in brucellosis enlargement of various superficial lymph nodes may occur as a specific manifestation. From this analysis it is not possible to show a clear relationship between glandular enlargement and the different varieties of Brucella or that there is convincing evidence of local regional adenitis in relation to the port of entry of the organism. In a number of instances the lesions appear to be specific. Brucellosis, because of the prolonged undulating fever, palpable spleen, palpable lymph nodes and eosinophilia, may be easily confused with Hodgkin's disease, and especially as the cellular reaction in the lymph nodes of Brucella infection may on occasion resemble that seen in certain cases of Hodgkin's disease.

## Archives of Dermatology and Syphilology, Chicago

**45**:1037-1250 (June) 1942

Dermatitis Due to Blossom of Grevillea Banksii: Newly Recognized and Common Entity in Hawaii. H. L. Arnold Jr., Honolulu, Territory of Hawaii.—p. 1037.
Dermatitis Due to Transparent Adhesive Tape. H. Keil, New York, and E. S. Bereston, Baltimore.—p. 1052.
Dermatitis of Eyelids Due to Philodendron (Scandens Cardatum) Plants. J. H. Harris, New York.—p. 1066.
Cutaneous Manifestations of Internal Malignant Tumors. S. W. Becker, D. Kahn and S. Rothman, Chicago.—p. 1069.
Lichen Planopilaris: Lichen Planus et Acuminatus Atrophicans (Feldman) and Lichen Spinulosus and Folliculitis Decalvans (Little). W. Sachs, Jersey City, N. J., and G. De Oreo, Cleveland.—p. 1081.
Electrolysis: Introduction of Instrument for Relatively Painless Treatment. E. A. Hand, Saginaw, Mich.—p. 1094.
Rational Prescription Writing in Dermatology. H. Goodman, New York.—p. 1101.
*Dermatophytosis of Hands: Diagnosis and Prognosis. E. Epstein, Oakland, Calif.—p. 1113.
Deproteinated Pancreatic Extract in Treatment of Psoriasis. J. G. Downing, E. A. Glicklich and S. J. Messina, Boston.—p. 1125.
Hemochromatosis: Report of Case and Comment on Methods of Making Definite Diagnosis. A. A. Humphrey, S. Alpiner and L. E. Verity, Battle Creek, Mich.—p. 1128.
Geographic Distribution of Lupus Erythematosus. E. Gahan, New York.—p. 1133.
History of Chicago Dermatologic Society. M. S. Wien, Chicago.—p. 1138.
Pseudoxanthoma Elasticum with Angioid Streaks: Syndrome of Groenblad and Strandberg. S. H. Silvers, Brooklyn, and H. E. Wolfe, New York.—p. 1142.
Colloid Milium: Vitamin Deficiency Disease? S. C. Way, San Francisco.—p. 1148.
Pigmentation of Skin Due to Vitamin A Deficiency: Report of Case and Review of Literature. J. A. Tolmach and T. N. Graham, New York.—p. 1156.

**Dermatophytosis of Hands.**—Systematic mycologic examination of 196 unselected patients with inflammatory lesions of the hands seen in private practice was instituted by Epstein, who demonstrated typical hyphae in 5.6 per cent and in 7.8 per cent of the 142 selected for treatment. The eruptions of these 142 patients could be divided into the following groups: 1. The squamous type cleared easily and showed no tendency toward recurrence. 2. The vesicular type responded rapidly but tended to recur. 3. The hyperkeratotic type was resistant to therapy. 4. There were also a few mixed and unclassified types. It is concluded that the diagnosis of dermatophytosis of the hands must rest on laboratory investigation.

## Archives of Neurology and Psychiatry, Chicago

**47:**879-1106 (June) 1942

Regulation of Cerebral Carbon Dioxide. E. L. Gibbs, F. A. Gibbs, W. G. Lennox, Boston, and L. F. Nims, New Haven, Conn.—p. 879.
*Epidermoid, Dermoid and Teratomatous Tumors of Central Nervous System. W. T. Peyton and A. B. Baker, Minneapolis.—p. 890.
Pathologic Changes in Central Nervous System in Experimental Electric Shock. Gert Heilbrunn and A. Weil, Chicago.—p. 918.
Encephalographic Ratio for Estimating Ventricular Enlargement and Cerebral Atrophy. W. A. Evans Jr., Detroit.—p. 931.
Fatal Infectious Polyneuritis in Childhood: Infectious Neuronitis, Acute Polyneuritis with Facial Diplegia, Guillain-Barré Syndrome and Landry's Paralysis. C. D. Aring and A. B. Sabin, Cincinnati. —p. 938.
*Familial Mental Deficiency Akin to Amaurotic Idiocy and Gargoylism: Apparently New Type. G. A. Jervis, Thiells, N. Y.—p. 943.
Alternating Tremor and Its Relation to Cortical Pathways. B. H. Balser, New York.—p. 962.
Studies on Corpus Callosum: III. Contribution to Study of Dyspraxia and Apraxia Following Partial and Complete Section of Corpus Callosum. A. J. Akelaitis, W. A. Risteen, R. Y. Herren and W. P. Van Wagenen, Rochester, N. Y.—p. 971.
*Disturbances in Brain Function Following Convulsive Shock Therapy: Electroencephalographic and Clinic ' Studies. N. A. Levy, H. M. Serota and R. R. Grinker, Chicago.—p. 1009.

**Tumors of Central Nervous System.**—Peyton and Baker report 9 cases of epidermoid, 1 of dermoid and 4 of teratoma of the central nervous system. They belong to the tumors of mixed tissue which arise from cell rests. When the neoplasm contains tissues from all three germ layers it is a true teratoma, when of mesodermal origin it is called a dermoid cyst, and the epidermoid, the most common, is composed of only the ectoderm layer of tissue. The intracranial epidermoid is cured by surgical removal; operation may be followed by aseptic meningitis; the tumor may be calcified; when it is in the lateral ventricle it produces a characteristic encephalogram, from which not only is the tumor located but it is recognized as an epidermoid. Bilateral intraventricular cholesteatoma similar to that frequently found in the horse occurs also in the lateral ventricles of man. The following are the characteristics of dermoid and teratoma: they are associated with dysraphia; they are slowly progressive lesions of the cord or cauda equina, and they produce, by pressure erosion, dilatation of a long segment of the spinal canal.

**Familial Mental Deficiency.**—Jervis reports 6 cases of familial mental deficiency characterized by severe idiocy, stunted growth, characteristic facies and peculiar changes in the bones of the skull. He believes that these represent a new type. Pathologically there is ubiquitous swelling of the nerve cells with cytoplasmic infiltration of lipoid granules. There are differences in this condition and in the juvenile amaurotic idiocy and gargoylism which appear to justify a separation of this type of mental deficiency. However, the three conditions show obvious similarities which warrant their inclusion in the same group of diseases. In the pathogenesis of this condition the morbid process is considered an instance of localized lipidosis. Etiologically the disease is believed to be genetically determined and, probably, inherited through recessive genes.

**Disturbances in Brain Function Following Shock Therapy.**—Electroencephalograms ("global" recordings of brain potentials) were recorded by Levy and his associates before the first convulsive shock treatment and at varying times up to several months after treatment of 23 patients was discontinued, all but 4 of whom were suffering from primary or secondary affective disorders. Of the 4, 2 were schizophrenic, 1 was paranoid with depression and 1 was schizophrenic with no significant disturbance in mood. In all the patients evidence of neurologic disease was absent. Sensorial and intellectual disturbances of the "organic" type were absent in all before treatment. The presence and extent of post-therapeutic disturbances in cerebral function were determined. Fourteen of the patients recovered or improved and 9 had early relapses or did not improve. Evidence of disturbed cerebral function, indicated by changes in the electroencephalogram and by changes in intellectual function, was present, respectively, in 50 and 45 per cent. Signs of epileptoid disturbances (3 per second waves, bicuspid and dicrotic waves, spike and wave formations and greatly increased amplitude) were evinced in the electroencephalograms of the most severely affected patients. The post-therapeutic clinical evidence of impaired cerebral function consisted of an "organic" type of sensorial and intellectual impairment. Recovery from these disturbances usually occurred in a few weeks, in the more severely affected patients sometimes in as long as six months. Clinical recovery or improvement was apparently not dependent on the presence of these electroencephalographic changes.

## Arkansas Medical Society Journal, Fort Smith

**38:**249-268 (May) 1942

Control of Estrogenic Therapy During the Menopause with Vaginal Smears. J. H. Hellums, Dumas.—p. 249.
Geriatrics: General Remarks on Care of the Aged. R. H. Johnston, Clarksville.—p. 253.

**39:**1-44 (June) 1942

The Medical Profession: Its Opportunities for Service Today. H. F. H. Jones, Little Rock.—p. 1.

## California and Western Medicine, San Francisco

**56:**333-384 (June) 1942

Intravenous Anesthesia in the Field. J. M. Rigdon, Fort Ord.—p. 337.
Wartime Problems in Industrial Health. C. M. Peterson, Chicago.—p. 339.
Hallucinations: Their Mechanism and Significance. J. A. Cutting, Agnew.—p. 342.
Endocrine Therapy: Potential Abuses in Gynecologic Disorders. C. F. Fluhmann, San Francisco.—p. 345.
Sulfonamide Medication. L. A. Rantz, San Francisco.—p. 347.
Intestinovesical Fistula. R. W. Barnes and M. R. Hill, Los Angeles. —p. 350.
Anuria Due to Sulfadiazine Crystals: Report of Case. A. L. Mollath, E. Belt and C. E. Ebert, Los Angeles.—p. 355.

## Kentucky Medical Journal, Bowling Green

**40:**201-248 (June) 1942

Treatment of Burns. R. A. Griswold, Louisville.—p. 203.
Local Treatment of Burns. J. E. Hamilton, Louisville.—p. 207.
Primary Treatment of Compound Fractures. K. A. Fischer, Louisville. —p. 212.
Treatment and Care of Varicose Veins. J. E. Haynes, Dawson Springs. —p. 214.
Early Symptoms of Carcinoma in Colon and Rectum. I. Abell Jr., Louisville.—p. 219.
Developments in Medicine, National, Economic and Scientific. F. H. Lahey, Boston.—p. 224.
Tularemia. R. G. Webb, Livingston.—p. 228.
Six Thousand Spinal Anesthesias. C. C. Howard, Glasgow.—p. 230.
Sphere and Clinical Application of Radiation Therapy. D. Y. Keith, Louisville.—p. 234.
Advantages of Direct X-Ray Therapy. J. Love, Louisville.—p. 238.

## Minnesota Medicine, St. Paul

**25:**425-520 (June) 1942

Health and Safety of Wartime Workers. L. D. Bristol, New York.—p. 441.
Legal Aspects of First Aid by Lay People. C. J. Potthoff and P. Carroll, Minneapolis.—p. 448.
Prevention of Automobile Accidents. M. N. Walsh, Rochester.—p. 451.
Mechanism of Uveitis. E. W. Hansen, Minneapolis.—p. 455.
*Nasal Sinusitis and Orthostatic Albuminuria in Childhood. W. R. Shannon, St. Paul.—p. 458.
Medicolegal and Sociologic Aspects of Diabetes Mellitus. A. H. Beard, Minneapolis, and J. A. Layne, Great Falls, Mont.—p. 460.
*Histaminase in Treatment of Urticaria and Other Dermatoses. C. W. Laymon, Minneapolis.—p. 466.

**Nasal Sinusitis.**—Shannon calls attention to the fact that orthostatic or postural albuminuria in children is a frequent accompaniment and apparently a result of nasal sinusitis, especially of a subacute or chronic type. Therefore such albuminuria must be viewed with much more concern than has been the custom heretofore.

**Urticaria and Other Dermatoses.**—Since his first report in 1939 on the use of histaminase for various dermatoses, Laymon has continued to use the drug and now adds the following data: Of 35 cases of urticaria, 21 were clinically cured and 14 were not benefited; there was no appreciable improvement in 7 cases of acne vulgaris, in 2 of dermographism or in 11 of atopic dermatitis, and the light sensitization dermatitis of 1 patient definitely improved. The daily dose varied from 60 to 120 histamine detoxifying units. The urticaria of the patients selected for treatment was of relatively long duration and had proved refractory to the usual therapeutic measures.

## FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

### Annals of Rheumatic Diseases, London

**3**:1-76 (May) 1942

War on Rheumatism. Horder.—p. 1.
Hemolytic Streptococcus Infections and Acute Rheumatism. C. A. Green.—p. 4.
Generic and Specific Influences of Nutrition in Total Support of Arthritics. R. Pemberton and C. W. Scull.—p. 42.
Fibrositis: Biographic Study of Fifty Civilian and Military Cases from the Rheumatic Unit, St. Stephen's Hospital (London County Council), and a Military Hospital. P. Ellman, O. A. Savage, E. Wittkower and T. F. Rodger.—p. 56.

### British Journal of Ophthalmology, London

**26**:189-240 (May) 1942

Etiology of Phlyctenular Ophthalmia. A. Sorsby.—p. 189.
Involuntary Convergence, Eyestrain and Squint. N. A. Stutterheim. —p. 216.

### British Medical Journal, London

**1**:573-600 (May 9) 1942

Medicine and Public Welfare. Dawson.—p. 573.
Estimation of Prothrombin with Venom and Lecithin. L. J. Witts and Felicity C. G. Hobson.—p. 575.
Perineuritis. J. Cyriax.—p. 578.
Massive Blood Loss: Recovery. S. Way and F. Robertson.—p. 581.
Ariboflavinosis: Reports of Two Cases. G. Duckworth.—p. 582.

**1**:601-630 (May 16) 1942

*Inhibition of Lactation by Synthetic Estrogenic Substances, with Special Reference to Dienestrol. Josephine Barnes.—p. 601.
New Aspect of Dry Pleurisy. J. Smart.—p. 604.
*Vitamin $B_1$ in Urine and Placenta in Toxemia of Pregnancy. W. C. W. Nixon, Margaret D. Wright and E. C. Fiefler.—p. 605.
Subarachnoid Hemorrhage in Identical Twins. J. G. O'Brien.—p. 607.
Urea and Its Effect on Tubercle Bacilli. S. L. Cummins.—p. 609.

**Control of Lactation with Estrogen.**—Barnes tested the effects of the new synthetic estrogen γδ-di-*p*-hydroxyphenyl-Δ$^{\beta\delta}$-hexadiene, known as "dienestrol," for inhibiting lactation and compared them with that of diethylstilbestrol and the synthetic estrogenic substance hexestrol in 134 patients who lost their fetus because of stillbirth, abortion or neonatal death, and sometimes in unmarried mothers who had to "foster" their children or in a few mothers with extremely sore breasts and severely cracked nipples. No other treatment was given. Ultimate success was achieved in all cases, though in some treatment was repeated. The course of treatment usually lasted five days; 81 received diethylstilbestrol, 37 dienestrol and 16 hexestrol. The results with dienestrol were apparently not as good as those with diethylstilbestrol, but this was partly accounted for by the fact that it was at first given in small doses (smaller than the initial 5 mg. of diethylstilbestrol twice a day diminished by 1 mg. each day). The optimal total dose of dienestrol was 2 to 3 mg. in five days. The small dose tried at first—0.1 mg. twice daily for five days—was inadequate. The most satisfactory results were obtained with an initial dose of 0.5 mg. twice a day diminished by 0.1 mg. each day. The results were better when treatment was begun within one day of delivery than if started later. They were also better in patients in whom pregnancy had advanced beyond thirty-two weeks than in those in the earlier months of pregnancy. After treatment was stopped on the fifth day the breasts of about a fourth of the patients filled up and further treatment was necessary, but ultimate success was achieved in each one. Three patients with engorged breasts were treated successfully while lactation continued normally. No ill effects followed treatment except that 3 patients complained of transient nausea.

**Vitamin $B_1$ and Pregnancy Toxemia.**—The state of vitamin $B_1$ nutrition of 106 pregnant women was based by Nixon and his colleagues on the twenty-four hour urinary excretion of the vitamin. The collection began on their admission to the hospital. The vitamin $B_1$ content of the placenta of certain of these patients was also examined. The pregnancies of 46 were clinically normal and of 60 they were abnormal; 6 had hyperemesis, 28 hypertension, 3 preeclampsia, 9 eclampsia and 14 edema. In those with eclampsia the amount of vitamin $B_1$ excreted in the urine on admission to the hospital was significantly lower than in those having a normal pregnancy; and the concentration of vitamin $B_1$ in the placenta was also significantly lower than that of the placenta of normal pregnancy. In view of these observations and the occurrence of edema and suppression of urine in eclampsia, which offers a striking similarity to the clinical picture of beriberi, it is suggested that vitamin $B_1$ therapy might be beneficial for such patients. In hypertension the urinary excretion of the vitamin was normal, but in hyperemesis and edema it was even lower than that in preeclampsia, which was 2.86 international units as compared to 3.39 in the normal pregnancies.

### Lancet, London

**1**:523-550 (May 2) 1942

Postoperative Administration of Fluids to Children. G. M. Arnott and W. F. Young.—p. 523.
*Sulfonamides by Mouth in Treatment of Impetigo. B. E. Schlesinger and N. H. Martin.—p. 527.
*Antigenic Properties of Hemophilus Pertussis in Relation to Active Immunization. D. G. Evans.—p. 529.
Cetyltrimethylammonium Bromide: New Disinfectant and Cleaning Agent. J. M. Barnes.—p. 531.
Middle Meningeal Hemorrhage After Head Injury Without Fracture of Skull. M. A. Falconer and F. Schiller.—p. 532.

**Sulfonamides by Mouth in Treatment of Impetigo.**—The successful results following oral administration of sulfanilamide, sulfapyridine, sulfathiazole or sulfadiazine to 141 male patients with impetigo prompts Schlesinger and Martin to report their work. At first 18 Gm. of the sulfonamide was given in four days, but as certain patients required further treatment the dose was increased to 24 Gm. given in five or six days. During treatment all patients were kept in bed. No local treatment was used. Most patients treated with sulfanilamide, sulfapyridine or sulfathiazole were depressed, in contradistinction to those receiving sulfadiazine, who exhibited no depression. Neutropenia did not develop. During a successful course of treatment the lesions dried up in thirty-six to seventy-two hours. In the next twenty-four to forty-eight hours the crusts fell away, leaving a flushed surface which disappeared gradually and the skin returned to normal. Twenty-six of the 50 patients treated with sulfanilamide were cured, as were 21 of 35 treated with sulfapyridine and 38 of 46 with sulfathiazole and 8 of 10 with sulfadiazine. Failure was due to well defined causes: autoreinfection, chronic impetiginized fissures, fomes and mild sycosis. However, these conditions cleared up on local treatment with the sulfonamides. Of 29 patients with infected scabies, furunculosis and sycosis who were also treated with sulfonamides by mouth, 13 were cured and 4 were improved. Sulfathiazole and sulfadiazine appear to be the drugs of choice, but when streptococci are the predominating organisms sulfanilamide or sulfapyridine are almost as satisfactory, provided adequate concentrations are maintained.

**Antigenic Properties of Hemophilus Pertussis.**—Evans carried out experiments on rabbits to determine whether the pertussis vaccines now used in the prophylaxis of whooping cough are capable of stimulating the production of antitoxin. The strain of Hemophilus pertussis used had been preserved in the dry state in vacuo since its isolation and was in the phase 1 and fully toxigenic condition. All preparations were made from bacilli grown on Bordet-Gengou medium for forty-eight hours. The experiments reveal that a toxic extract of Hemophilus pertussis, obtained by disruption of bacilli by physical methods, when detoxified with formaldehyde produces an antitoxin and antibacterial antibody on injection into rabbits. A suspension of whole bacilli treated with formaldehyde did not act this way but only produced an antibacterial antibody, as did heated bacilli and heated extract. It is suggested that any investigation into new types of vaccine for prophylactic immunization against whooping cough should consider the significance of the toxin in infection and the value of toxoid as an immunizing agent. By using a vaccine capable of stimulating the production of antitoxin in addition to antibacterial antibody, a more complete protection may be established than that which has been obtained heretofore.

### Tubercle, London

**23**:59-82 (March) 1942

Bronchoscopic Investigation and Treatment of Experimental Cases of Phosgene Poisoning in Goats. J. E. G. McGibbon.—p. 59.
Some Reflections on the Tuberculous in Industry. B. Mann.—p. 72.

## Schweizerische medizinische Wochenschrift, Basel

**72:**141-176 (Feb. 7) 1942. **Partial Index**

Tuberculous Postprimary Initial Complexes. P. Schwartz, Rosa Rössler and C. Arkayin.—p. 141.
Primary Tuberculous Infections in Adolescents and Adults. S. J. Leitner.—p. 145.
Specific Early Diagnosis of Tuberculosis of Bones and Joints. F. Cevey. —p. 152.
*Conservative Cure of Renal Tuberculosis. W. Hofmann.—p. 154.
Pleuroscopy and Separation of Adhesions: Present Possibilities of Complete Liberation of Pulmonary Stump by Endopleural Route. R. Jeanneret and A. Gilliard.—p. 156.
Causes of Avoidable Failures of Collapse Therapy. W. Frochlich.—p. 159.
*Demonstration of Tubercle Bacilli in Direct Smears with Osol Staining in Dark Field as Method of Choice. H. Egli.—p. 166.

**Conservative Cure of Renal Tuberculosis.**—According to Hofmann, cure of renal tuberculosis by a conservative regimen is generally denied. Cicatrization of tuberculous foci with preservation of kidney function has been observed only twice, and in 1 of these cases exact anatomic study had not been made. Aside from the autonephrectomies, in which autoexclusion of the diseased kidney may take place, there may occur intrarenal shutting off of tuberculous foci. Both processes may simulate a clinical cure, since in either case the tuberculous focus is shut off from the renal pelvis and the discharging renal passages. Pyuria and tubercle bacilli disappear from urine, and the tuberculous lesions in the bladder subside. The subjective condition of the patient may improve to such an extent that a cure is assumed. Clairmont and Schaffhauser observed 3 such cases in which the encapsulated foci gave rise to fresh tuberculous dissemination three years later. These authors advocate the removal of such foci even in the absence of symptoms. Hofmann believes that such temporary exclusions of tuberculous foci in the kidney are extremely rare. He reported in 1925 a case of renal tuberculosis in which a cure had been obtained under conservative treatment. The man had rejected a suggestion for the removal of the right kidney in 1920 and had been placed on a conservative regimen of sun baths, fresh air and tuberculin injections. He felt well in 1921 and the urine was free from tubercle bacilli. In 1924 tuberculosis of the left epididymis was detected, but the urine and bladder were normal. The left testis and epididymis were removed, following which the genitourinary apparatus appeared to be free from lesions. In 1926 the man developed pulmonary lesions, and in 1932 bladder symptoms recurred and tuberculosis of the prostate was discovered. While the bladder urine was positive, the renal urine remained negative, suggesting that the bacilli in the bladder urine had their origin in the prostate. Following treatment at a sanatorium the symptoms subsided and the patient felt comparatively well. Later examination indicated that the pulmonary lesions had healed. Examination of the bladder urine in 1938 indicated that the tuberculosis of the prostate had healed. Clinically the patient is free from symptoms at the age of 71. The author agrees with Wildbolz that a cure of renal tuberculosis cannot be proved without an accurate anatomic study. He believes that in his case intrarenal exclusion is perhaps more likely than a cure. It is also apparent that the tuberculous infection was of an extremely mild type.

**Demonstration of Tubercle Bacilli.**—Egli points out that Osol in 1927 described a staining method with thick smears which yielded much better results than the Ziehl-Neelsen method. Hagemann in 1937 recommended fluorescence microscopy for the demonstration of tubercle bacilli, demonstrating that the method was much more effective than the Ziehl-Neelsen method. Pothmann found that the results with fluorescence microscopy could be paralleled by the dark field method utilizing the Osol staining instead of the Ziehl-Neelsen. He demonstrated the great superiority of the Ziehl-Neelsen dark field method over the Ziehl-Neelsen light field method but found that in the dark field Osol's stain is superior to Ziehl-Neelsen's. Egli reports his own comparative studies on 310 specimens (sputa, laryngeal, gastric, pleural, urinary and pus specimens). He concludes that: 1. The expensive and relatively difficult fluorescence method can be used for the demonstration of tubercle bacilli only in scientific institutes. Its results are not better than those obtained with the Osol stain in the dark field method. 2. The Osol dark field method is six times more accurate than the ordinary Ziehl-Neelsen method as regards the detected number of bacilli and as regards the time factor. 3. The dark field equipment requires few installations and is only about one tenth as expensive as is the fluorescence equipment and is easy to handle. 4. Osol's staining technic is simple and resembles the Ziehl-Neelsen method.

## Revista de la Asoc. Méd. Argentina, Buenos Aires

**56:**125-182 (March 15-30) 1942. **Partial Index**

*Cervicosubdural Sympathogonioma in the Child: Case. R. Cibils Aguirre, D. Brachetto-Brian, C. M. Casco and J. A. Tahier.—p. 125.
Local Sulfanilamide in Surgery. A. Wybert and L. A. Uslenghi.—p. 149.

**Cervicosubdural Sympathogonioma in the Child.**—Cibils Aguirre and his collaborators report the case of a child 3 years old with symptoms of progressive compression of the spinal cord. Roentgenography revealed a tumor in the upper portion of the vertebral canal. At the operation an intradural tumor compressing the first, second and third segments of the spinal cord was found. There were no metastases. The tumor was free, isolated and encapsulated in fibrous and connective tissue containing neoplastic cells. Compression of the cord resulted in death early in the course of the development of the tumor. Microscopic study revealed that the tumor was a sympathogonioma. The authors believe that their case is the first of this localization and type.

## Revista Española de Tuberculosis, Madrid

**9:**609-668 (Sept.) 1940. **Partial Index**

Allergy in Tuberculosis: Local Leukocytic Formula in Normal and Desensibilized Skin. J. Zapatero Domínguez and E. López Gutiérrez. —p. 609.
*Supernumerary Cervical Ribs. T. Cerviá and J. de la Rosa.—p. 627.
Pathogenesis and Therapy of Pulmonary Perforation. E. Regli Fernandez.—p. 642.

**Cervical Ribs.**—Cerviá and de la Rosa studied 1,678 roentgenograms of the thorax of persons of either sex, who were observed in an antituberculosis dispensary. Cervical ribs were found in 115 (47 men and 68 women). The abnormality was unilateral in 22 and bilateral in 93. Six unilateral ribs were on the right side and sixteen on the left. The bilateral ribs were of the same size on both sides in 65, the right rib was longer than the left in 15 and the left was longer than the right in 11. The abnormality was found in 24 children, 44 persons between 11 and 20 years of age, 23 persons between 20 and 30 years of age and 23 between 30 and 50 years of age. None of the patients complained of symptoms. The abnormality was familial in 3 instances: a father with a unilateral cervical rib with 3 children with bilateral cervical ribs, 2 children (brother and sister) with bilateral cervical ribs and 4 adult brothers with either unilateral or bilateral cervical ribs.

## Therapie der Gegenwart, Berlin

**82:**97-144 (March) 1941. **Partial Index**

Question of Necessity for Therapy in Sports Heart. G. W. Parade. —p. 97.
Therapy of Maxillary Gunshot Wounds, with Special Reference to War Wounds. H. Hammer.—p. 100.
Technic, Indications and Results of Fever Baths. F. Walinski.—p. 106.
Feeding of Premature Infants. K. Schwartzer.—p. 110.
Sulfanilamide Derivatives and Supplementary Therapy of Epidemic Meningitis. G. Säker.—p. 116.
*Treatment of Erythema Nodosum. J. Simon.—p. 142.

**Treatment of Erythema Nodosum.**—Simon reports the clinical history of a girl aged 22 who five days before entering the hospital developed an eruption on the legs, fever and chills. Examination revealed cutaneous infiltrations 38 mm. in size and bluish red discolorations on the legs and later on the arms. The disorder was diagnosed as erythema nodosum. Dietetic treatment and medication with acetylsalicylic acid had no effect; further efflorescences developed. Azosulfamide was given and after two days of this therapy the erythema became paler and disappeared completely after four days. Five days later the patient could get up and had no more complaints.

# Book Notices

**Carcinoma and Other Malignant Lesions of the Stomach.** By Waltman Walters, B.S., M.D., M.S. in Surgery, Professor of Surgery, University of Minnesota (Mayo Foundation), Minneapolis, Howard K. Gray, B.S., M.D., M.S. in Surgery, Associate Professor of Surgery, University of Minnesota (Mayo Foundation), James T. Priestley, B.A., M.D., M.S. in Experimental Surgery, Associate Professor of Surgery, University of Minnesota (Mayo Foundation), and Associates in the Mayo Clinic and Mayo Foundation, Rochester, Minnesota. Cloth. Price, $8.50. Pp. 576, with 152 illustrations. Philadelphia & London: W. B. Saunders Company, 1942.

This book of twenty-three chapters, contributions to which were made by fourteen of the authors' associates on the Mayo Clinic staff, is a thorough discussion of all phases of the problem of cancer of the stomach. Coming from a medical center which possesses such rich material and dealing with a disease which has an alleged annual toll of 38,000 persons in the United States, it combines reviews of experimental data, clinical opinions based on experience, and statistical evidence from which tenets of etiology, diagnosis and treatment may be formulated and clarified.

On the side of etiology, the relationship of gastritis to carcinoma, a vital topic of present day discussion, is treated by Morlock and Hartman in their chapter on Recognition of Malignant Lesions of the Stomach, whose opinion it is that "it is just as important to keep patients with gastritis under a period of continuous observation as it is to do so with patients suffering from a small circumscribed ulcerating gastric lesion who are not subjected to immediate exploratory operation—this applies particularly to the atrophic and the severe hypertrophic ulcerative forms of gastritis." Eusterman, in his highly interesting chapter on Special Laboratory Observations, discussing the causes of changes of gastric secretion in gastric carcinoma, says "Gastritis as a precursor would best explain the achlorhydria and low secretory volume in the presence of small or early lesions." Yet from this same source of material, but from a pathologic angle, MacCarty, in the chapter on Surgical Pathology States, says "Carcinoma of the stomach arises in the mucosa of the borders of chronic gastric ulcers, in adenomatous polyps and theoretically in the mucosa in chronic gastritis. For this last possibility, I have seen no pathologic evidence. These statements are based on studies of stomachs resected for chronic gastric ulcers, adenomatous polyps, carcinomas and chronic gastritis."

The manifold problems of diagnosis are treated in several articles. Important among the suggestions for differentiation of the malignant from the benign lesion are two emphasized by Morlock and Hartman: (1) that the patient with a healed gastric lesion be resurveyed at regular intervals and (2) that recurrence of a gastric lesion be suspected of malignancy. Kirklin's chapter on Roentgenology, with its twelve instructive illustrations, is a concise exposition of the chief criteria of roentgenologic diagnosis of the early carcinoma. His discussion of the difficulties of diagnosing "specifically and confidently" the small pyloric or prepyloric carcinoma will evoke sympathetic understanding from all gastroenterologists, who are so often baffled by this problem. Moersch has a chapter on gastroscopy, with several excellent reproductions of typical lesions as seen through the gastroscope.

One of the most interesting chapters is Snell's—The Physiologic Consequences of Gastric Carcinoma and of Gastrectomy—in which he discusses both the preoperative problems of anemia, protein depletion and chemical disturbances due to pyloric obstruction and vitamin deficiency states as well as the metabolic and nutritional disturbances continuing in the postoperative state or developing after gastric resection. His experience indicates that nutritional edema as a result of depletion of plasma proteins does not often reach levels that are clinically important either in the preoperative or in the postoperative state, and in the few such cases arising from long standing pyloric obstruction observed at the Mayo Clinic one or two blood transfusions have sufficed to correct the condition speedily. This chapter is a brief and very useful review of modern conceptions of the blood chemistry and nutrition as applied to the stomach in health and disease.

From the angle of treatment, almost four fifths of the volume deals with indications for surgery, surgical technic and the results and prognosis of surgical cases. In the discussion of indications for surgery there is emphasis on the rewards of exploratory operation even when roentgenologic indications are discouraging in cases in which there is no evidence of metastatic extension. Resection could actually be done in 14.3 per cent of 488 cases in which inoperability was diagnosed roentgenologically. It is also pointed out that the duration of symptoms does not constitute "an accurate indication regarding the size, location, grade or extension of the growth." Rivers' chapter on "Counteracting Dehydration, Retention and Toxemias of Gastric Stasis" is a practical guide for preoperative measures. There are seven chapters on surgical technic, including the technic of the operating room and of anesthesia, with two chapters on Billroth I resection and the Billroth II with Hofmeister and Polya modifications, all so detailed and well illustrated that they will undoubtedly serve most usefully as surgical textbooks. A special chapter is devoted to Total Gastrectomy with a careful analysis of indications and with the deduction that although the mortality rate is high (31 per cent) and the survival time short (none reported over five years) the improvements during the survival years have been excellent. There is a short chapter by Desjardins on Roentgenologic Treatment, indicating its restriction to inoperable cases and designating the selected cases in which improvement may be expected. The final chapter, on Prognosis and End Results, contains statistics calculated to show operability of the lesions, operability related to age of patient and gastric acidity, mortality after operation and survival rates classified with relation to (1) grade of malignancy, (2) age of patient, (3) gastric acidity and (4) location of lesions. An appendix contains statistical tables and graphs and an excellent index which complement this book of knowledge and experience on a disease about which neither the public nor physicians should allow themselves to become either pessimistic or careless, lest an opportunity be missed for early detection and cure or at least temporary abeyance.

**La enfermedad diverticular de la próstata: Su estudio como "infección focal" de la próstata.** Por el Dr. Alberto E. García. Tesis de doctorado, Universidad nacional de Buenos Aires, Facultad de ciencias médicas. Paper. Pp. 140, with 103 illustrations. Buenos Aires: Librería y Editorial L. E. Y. C. A., Nocito & Rañó, 1942.

This impressive well printed monograph contains ninety-five urethrograms, ten anatomic sketches, nine photomicrographs, three photographs of gross specimens and seven full color plates, all with clinical correlations. The author's fundamental interest in latent foci of infection led him to study diverticular disease of the prostate. The essential pathologic anatomy of the disease consists in multiple septic prostatic cavities which communicate with the posterior urethra and thus keep up the infection indefinitely. Its understanding and study have been possible through urethrograms. By this medium the author was able to appreciate the true pathologic significance of these septic foci. Two local conditions favor the persistence of the infection: (*a*) attenuated virulence of the organisms, (*b*) inadequate drainage. Gonorrhea is the most frequent primary cause, but when the condition is well developed this cannot be proved.

Local symptoms are slight. The patient nearly always comes for advice regarding general symptoms or for complications. The systematic evolution of the disease may be described in three stages: (1) primary infection of the prostate, (2) latent period and (3) complications and sequalae, local and general. The author reports 1 case of acute fatal septicemia of prostatic origin. Secondary lesions of the urinary apparatus are explained by the process of development of diverticulitis and peridiverticulitis. They are multiple and often give rise to sclerosis of the internal sphincter. Exact diagnosis by cystourethroscopy and urethrography is of incalculable value to the patient. Treatment is based on the attainment of full and free communications of the prostatic cavities with the posterior urethra. Endoscopic electrocoagulation carefully done in several stages will assist in this aim. Recommended instruments are carefully described and sketched. The work here presented is a valuable contribution to the study of diverticular disease of the prostate.

# Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

## DIFFERENTIAL DIAGNOSIS OF DERMATOPHYTOSIS

***To the Editor:***—**With the approach of warm weather I believe most physicians will be confronted with "foot fungus" cases to handle. I should like to know what efficacious medication we possess in treating cases of dermatophytid complicating epidermophytosis. I have been able to control the latter with common fungicides, but the pruritic papulovesicular dermatophytid eruption has been a terrible task to ameliorate. Just what is the proper way to handle such cases? I have also noticed cases of dermatophytid . . which close investigation of the toes did not reveal any fungous infection. How do you explain such a phenomenon?**

**A. S. Catinella, M.D., Mechanicville, N. Y.**

ANSWER.—The intensely pruritic papulovesicular eruption mentioned is probably not a dermatophytid. It seems too itchy and too resistant to treatment. The trichophytids and favids secondary to scalp involvement often clear up spontaneously when the original focus of infection improves. A more likely explanation is that the eruption complained of is a secondary allergic dermatitis due to the drugs used in treatment, a contact dermatitis. If the lesions composing it are small and superficial, the vesicles easily ruptured, leaving weeping surfaces, this is probably the case. Naturally the causative drug or other strong fungicides will only increase the distress of the patient. Such sensitization takes place frequently after treatment of dermatophytosis. Soothing applications such as Burow's solution, 6 to 10 per cent in water, applied as cool wet dressings are indicated until the oozing ceases. Then a calamine lotion made with rose water in place of lime water can be used, or zinc paste without salicylic acid. Soap and water should be avoided. The patient should cleanse with oil whenever necessary, but it is not often necessary. He should use the utmost gentleness in applying the lotion or paste and in cleansing, for rubbing is apt to cause renewed itching.

It is not rare to see cases with an eruption clinically indistinguishable from dermatophytosis of the feet and hands in which no fungi can be found by direct microscopic investigation of the scales or vesicle roofs. Some of these will show fungi by culture, others will not. All writers on the subject seem to agree that when the hands are involved, which is often the case, fungi are rarely found in the hand lesions. Cases are on record in which fungi were found on one foot, not on the other, though both were diseased. Pompholyx, first called cheiropompholyx by Hutchinson, is a disease occurring usually on the feet and hands, clinically and histologically identical, except for the absence of fungi, with the disease called dermatophytosis of the feet and hands. The difficulty in explaining the fact that an eruption of the feet caused by fungi is often succeeded by a similar eruption on the hands in which no fungi are found was explained by Bloch as an original focus of fungous infection succeeded by a dermatophytid on the hands. With this view S. L. Peck (Epidermophytosis of the Feet and Epidermophytids of the Hands, *Arch. Dermat. & Syph.* **22**:40 [July] 1930) is in full accord. He quotes three possible explanations offered by Bloch and Walthard:

1. The fungi may be saprophytes growing in an eruption of an entirely different etiology. This Peck discards because of the well established pathogenicity of many of these fungi, the beneficial effect on the disease of fungicidal and fungistatic drugs and the experiments of von Graffenried and of Peck, in which they caused typical outbreaks by infection with cultures of some of the fungi commonly found in the disease.

2. Epidermophytosis on the feet combined with a different disease on the hands, dyshidrotic or eczematoid. This is not likely, because the percentage of cases in which both areas are involved is entirely too high for coincidence. There must be a direct relation between the disease of the hands and that on the feet.

3. The lesions on the feet are primary, those on the hands secondary (epidermophytids). Von Graffenried first demonstrated that all cases of ringworm of the feet show a positive reaction to tricophytin. Peck obtained from the blood of 1 patient cultures of one of the fungi present in the lesions on the feet.

Peck's argument is a strong one, and his view has been accepted by most American dermatologists; but it has not been proved conclusively. It seems much easier to accept the first of Bloch's postulates, that the disease is pompholyx. The fungi are those already present in the skin of the feet, taking on new growth when the epidermis becomes more succulent under the influence of the pompholyx. The hands show no fungi because conditions there do not favor infection with fungi. Support for this position has been given recently by Sulzberger, Bauer and Hecht (Common Fungous Infections of the Feet and Groins, *Arch. Dermat. & Syph.* **45**:670 [April] 1942), who show that the infection present on the feet is seldom passed to other persons even by the most intimate contact. The groin infections are nearly all autoinfections from the foci on the feet. Nearly every one of us has such foci, remaining dormant for years. One must acknowledge that many of these fungi are potentially pathogenic; but that does not prove their etiologic relation to the disease under discussion.

## RHEUMATOID OR ANKYLOSING ARTHRITIS OF SPINE

***To the Editor:***—**A man aged 33 has had ankylosing spondylitis for several years. Attempts at treatment with a great variety of vaccines, injections and medicines have been unsuccessful. In October 1941 his hemoglobin was 36 per cent. After three blood transfusions his hemoglobin was 57 per cent and his red cells 4,267,000. Two more transfusions raised the hemoglobin to 68 per cent. Finally it reached 80 per cent but is now falling. He states that the higher his hemoglobin, the more pain he has in his legs and back. Any suggestions would be appreciated.**

**C. Kenneth Cook, M.D., St. Paul.**

ANSWER.—Ankylosing spondylitis usually starts as a destructive arthritis of the sacroiliac joints with juxta-articular osteitis. Its cause is unknown. It affects men, chiefly young men, in a ratio of about fourteen men to one woman. As it progresses it produces painful spasms of the vertebral muscles, calcification of the vertebral ligaments (eventually producing the so-called bamboo spine in roentgenograms) and arthritis of the apophysial joints. In time notable spinal kyphosis and fixation of the chest wall may result unless appropriate therapeutic measures are taken. Involvement of peripheral joints is rare but involvement of the hips and shoulders may occur; the latter is usually periarticular (muscular) rather than intra-articular; however, the joint structures themselves may be affected.

Some students of arthritis attempt to distinguish ankylosing (rheumatoid) spondylitis from rheumatoid arthritis involving the spine. In the latter there is rheumatoid arthritis of the apophysial joints and often of the peripheral joints; subcutaneous fibrous nodules (absent in ankylosing spondylitis) may occur, but there is no ligamentous calcification, and the sacroiliac joints may or may not be affected (as they almost always are in ankylosing spondylitis). This distinction may be a real one but has not been accepted generally; at any rate the treatment of the two varieties is about the same.

The orthodox treatment of rheumatoid spondylitis involves the removal of obviously infected foci, daily use of professional or "home" physical therapy, perhaps fever reactions (typhoid vaccine) to induce lessening of muscular spasm, the use of postural and other spinal exercises, rib stretching and deep-breathing exercises to prevent or correct impending fixation of the chest and spine, the use of a bed with a firm mattress and a beaver board under the mattress to keep the spine straight at night, the use of one small or no pillow under the head, the use of a pillow between the scapulas or in the lumbar region for short periods during the day and night if kyphosis is developing. The patient may gain encouragement by making a monthly record of height and chest expansion. In selected cases the use of a Taylor brace during the daytime and a plaster shell or convex frame during the night gives considerable relief from pain and helps to prevent or correct the forward bending spinal deformity.

Recently Swain (*J. Bone & Joint Surg.* **21**:983 [Oct.] 1939) proposed the following plan: preliminary correction of spinal deformity by hyperextension in bed for two weeks, then the application of a plaster jacket "for early, continuous and adequate immobilization." Jackets were left on for weeks and replaced by new ones as the posture improved; they were worn by 62 patients for from several months to nine years. Swain reported that muscular spasm and pain were relieved rapidly, sleep was improved greatly despite the jacket, deformities were prevented or improved notably and expansion of the chest and weight increased.

Chrysotherapy (injections of gold salts) has given disappointing results. Still more recently Freyberg and his colleagues at Ann Arbor, Mich., recommended roentgen therapy as the remedy of choice to relieve pain (THE JOURNAL, Sept. 6, 1941, p. 826). Unfortunately roentgen therapy has not given relief to the patient in question.

If extensive ligamentous calcification has occurred it may be impossible now to obtain satisfactory correction of the spinal position by orthopedic and other measures, but if such calcifications are still absent, localized or minimal, much of the deformity may be due to correctible muscular spasms. Hypochromic anemia is a characteristic feature of most cases of rheumatoid arthritis or spondylitis. Its exact cause is not known, but distinguished hematologists (Minot, G. R.: *New England J. Med.* **208**:1285 [June 22] 1933. Haden, R. L.: *Arch. Phys. Therapy* **21**:671 [Nov.] 1940) have registered their inability to influence it materially by the usual measures for anemia. The idea "correct the anemia and the arthritis will improve" is fallacious. The anemia will lessen when the arthritis improves and probably not much before that time; hence no inordinate therapy need be directed against the anemia; an adequate diet, perhaps with ferrous sulfate as a supplement, and occasional transfusions are all that need be prescribed for the anemia. Acetylsalicylic acid is the safest and generally the most effective analgesic. Aminopyrine and cinchophen or neocinchophen are often effective substitutes, but one must be warned that granulocytopenia or cinchophen hepatitis occasionally results. Aside from the use of analgesics, pain may be relieved by the physical and orthopedic methods already mentioned.

This disease varies greatly in its duration and the speed of its progress. It may stop after a few months or it may progress slowly for years. The average duration of symptoms is about five to seven years. After the active disease stops, only painless residues remain. In a great many cases the spine may be stiff, but if it has been led to stiffen with the patient in the straight posture the resultant economic and physical disability may be very moderate.

## TOXICITY OF NITROGLYCERIN

***To the Editor:***—**I wish to ask for information or an available source of information regarding the industrial hazards and problems arising in workers in nitroglycerin. I have the ordinary care of employees in a powder plant and am confronted with the problem occasionally. I have been unable to find adequate reference to the literature of the past few years relative to this subject. I should like to ask the following questions: 1. What, if any, are the hazards to the circulatory or other systems of the body to long exposure to nitroglycerin? 2. What are the physical and other clinical findings of overexposure to nitroglycerin? 3. What, if any, are symptoms and signs of an accumulative action of nitroglycerin? 4. Are there any special clinical examinations indicative of circulatory damage from nitroglycerin? 5. In case of overexposure to nitroglycerin, what are the proper therapeutic measures? What physical standards should be adhered to in examinations of persons intending to work in nitroglycerin? Any help that you may be able to give on this subject will be sincerely appreciated.** **A. N. Shoun, M.D., Benson, Ariz.**

ANSWER.—Nitroglycerin, as employed industrially, is exquisitely toxic. The threshold for producing symptoms is so low as almost to defy measurement. The mere standing near a workman with traces of nitroglycerin or nitroglycerin powder on his body or clothing is quite sufficient to induce prompt manifestations. The commoner features are headache, throbbing in the head, palpitation of the heart, nausea, vomiting and flushing. The headache may be violent and may be associated with acute mania. This results from dilatation of the blood vessels about the brain, notably those of the meninges. This gives rise to such jargon terms as "dynamite head" or "powder headache." Always alcoholic drinks precipitate attacks and increase their severity. Nitroglycerin in industry commonly enters the body through inhalation of its vapors or through skin absorption. The families of workers may suffer from typical attacks shortly after the return to the home of nitroglycerin workers unless change of clothing and other precautions are carried out. Habituation is readily established, but this tolerance may disappear in as short a period as two days away from work. Nitroglycerin poisoning in industry is a characteristic "Monday disease." Although a few drops (3 to 5) may produce a fatality when taken internally, increases in exposure such as from 1 to 30 mg. may not produce highly different results. It may be doubted that any chronic type exists, although such forms have been described. No organic changes are known to arise in the heart, central nervous system or the eyes, although temporary blindness is common. The depressed blood pressure may return to normal within one hour after elimination of exposure. The disposition of compensation courts ordinarily is to deny any claims specifying prolonged disability. The enumerated questions of the general query are now answered:

1. Quick exposure rather than long exposure appears to be of greater significance.
2. Already answered.
3. Apparently there is no cumulative action of nitroglycerin.
4. In addition to features already mentioned, significance should be attached to low blood pressure and to polyuria. Occasionally ulcers about the fingertips arise, so that the fingers should be examined.
5. In instances of severe poisoning, oxygen should be administered along with intravenous saline solution and saline cathartics. Workers should be taught to preserve their habituation when away from work by carrying a few grains of powder under hatbands or somewhere about their person. However, this step is troublesome for members of the family and others about the worker. The only known cause for rejection of an applicant for nitroglycerin work apart from the usual causes for rejection is alcoholism. The following literature items furnish further data:

Ebright, G. E.: The Effects of Nitroglycerin on Those Engaged in Its Manufacture, THE JOURNAL, Jan. 17, 1914, p. 201.
Heitz, J.: Cardiovascular Status in Nitroglycerin Workers, *Arch. d. mal. du coeur* **17**: 578 (Sept.) 1924; abstr. THE JOURNAL, Oct. 18, 1924, p. 1279.
Solis-Cohen, Solomon, and Githens, Thomas Stotesbury: Pharmacotherapeutics, Materia Medica and Drug Action. New York, D. Appleton & Co., 1928.
McNally, W. D.: Toxicology, Chicago, Industrial Medicine, 1937.

## PREMATURE GRAY HAIR

***To the Editor:***—**A married white man aged 29 has recently developed loss of pigment of the nasal and temporal margins of the eyelashes of upper lids of both eyes. The central portions of these eyelashes are as yet uninvolved. Now this process is beginning to appear at the nasal part of the right eyebrow. The hair on the head is entirely free of this loss of pigment and there is considerable hypertrichosis of the body which also is uninvolved. There are some isolated pubic hairs which are white, obviously of recent acquisition. The history and physical examination are entirely negative: there is no evidence of any glandular or vitamin deficiency. Diet has been ample in all requirements. Can you suggest a diagnosis, etiology and treatment? Would para-aminobenzoic acid or the B complex be of any value, and, if so, what would be the proper dosage and where may the acid be obtained?** **M.D., Maryland.**

ANSWER.—Premature graying of the hair is an old problem without solution as yet. It is hard to explain the eccentricities of its occurrence, as in the example cited in the query. It is a familial peculiarity in many instances and in others is thought to result from nervous disturbances. It has long been suspected that deficient nutrition of nerves is a factor in its causation.

The vitamin studies which produce graying in animals and then cure it by correction of the diet have been made on mice, rats, dogs and silver foxes. By shaking a watery solution of liver extract, yeast or rice bran with fullers' earth the thiamine, riboflavin and pyridoxine are removed, leaving a solution of the "filtrate factor." Animals fed with a diet containing the other vitamins but lacking this factor soon show patches of fur that has become gray and thinned, ulcers sometimes appear on the tail or hind legs, the animal's skin becomes wrinkled as in old age, it becomes feeble, and it often dies within a few months if kept on the deficient diet. On adding the "filtrate factor" to the diet these symptoms clear up in most cases.

It is known that this factor contains pantothenic acid and para-aminobenzoic acid; but the effort to determine which of these is responsible for the prevention of graying has not been successful as yet, for there is disagreement among the research workers engaged in the problem. Ansbacher and his associates find that the lack of para-aminobenzoic acid causes the graying and that adding this vitamin to the diet restores the color of the depigmented patches. (Role of Para-Aminobenzoic Acid in the Vitamin B Complex—Studies with Mice, *Proc. Soc. Exper. Biol. & Med.* **48**:118 [Oct.] 1941). Others (Emerson, G. A.: Failure to Cure or Prevent Graying of Rats with Para-Aminobenzoic Acid, *ibid.* **47**:448 [June] 1941, Unna, Klaus; Richards, Grace V., and Sampson, W. L.: Studies on Nutritional Achromotrichia in Rats, *J. Nutrition* **22**:553 [Dec.] 1941) have succeeded in producing the gray spots by depriving the animals of pantothenic acid and have then cured the animals by adding this vitamin to their diet. It has been suggested that there may be other vitamins as yet undiscovered in the "filtrate factor."

Apparently there are only two articles in the medical literature dealing with the effects of vitamin B Complex and para-aminobenzoic acid on human hair. They are both by B. F. Sieve (Clinical Achromotrichia, *Science* **94**:257 [Sept. 12] 1941; The Clinical Effects of a New B Complex Factor, Para-Aminobenzoic Acid, on Pigmentation and Fertility, *South. Med. & Surg.* **104**:135 [March] 1942). When vitamin B complex was administered to 9 patients who were under treatment for endocrine dysplasias the gray hair of all, he reports, became noticeably darker. He then began the use of para-aminobenzoic acid for the same purpose, giving it to those on treatment with endocrine preparations and also to many who were on no other treatment. In his second paper he reports over 800 cases treated in this way. Within three to eight weeks of treatment

with the vitamin the gray hair became dirty yellowish and then "dark dusty gray."

These reports justify skepticism. As far as his articles show, Sieve's only evidence of color changes was his visual impressions. Those who have tried to judge slight color changes in the skin or hair realize how easily one can be deceived.

The question of the possible harmful action of para-aminobenzoic acid in large dosage must be considered. Several investigators have shown that this substance interferes in vitro with the bacteriostatic action of the sulfonamide drugs on pneumococci and staphylococci and that it promotes the growth of Streptococcus pyogenes (Spink, W. W., and Jermsta, Jean: Effect of Sulfonamide Compounds on Growth of Staphylococci in Presence and Absence of para-Aminobenzoic Acid, *Proc. Soc. Exper. Biol. & Med.* **47**:395 [June] 1941). Experiments on human beings with large doses of para-aminobenzoic acid should not be made until it is known what such interference with the bacteriostatic action of the sulfonamides signifies in the animal body.

## DISSEMINATED LUPUS ERYTHEMATOSUS

***To the Editor:***—**I should like your suggestions as to the diagnosis and treatment of acute lupus erythematosis disseminatus. What is known concerning the etiology of this condition and what measures best control the symptom complex?**

**G. H. Miles, M.D., Gallitzin, Pa.**

ANSWER.—The cause of this condition is not definitely known. Foci of infection, either streptococcic or tuberculous, may be underlying factors. The disease may follow the chronic discoid type or may occur as a primary acute systemic disorder. When it occurs as such, it is often difficult to diagnose.

The following symptoms commonly occur in the primary acute type: (1) edema of the face with an eruption on it resembling a severe toxic erythema or an erysipelas, (2) the presence of purpuric or erythema multiforme-like lesions on the hands, arms and various portions of the body, (3) erosions on the mucous membranes and glossitis, (4) joint pains, (5) fever of a septic type, (6) enlargement of lymph nodes, (7) leukopenia generally, (8) albuminuria, (9) a patchy or diffuse alopecia and (10) in terminal cases profound intoxication and delirium.

The disease has a high mortality, approximately 90 per cent. Fatal termination is generally due to pneumonia or nephrosis.

The treatment between attacks should consist of rest, avoidance of exposure to the sun, quinine by mouth, and cautious removal of suspected foci of infection. During attacks the patient should be kept in a quiet dark room, symptomatic therapy should be given for the symptoms that develop and blood transfusions and sodium thiosulfate intravenously may be administered.

The sulfonamide group of drugs may be tried, but so far they have not proved to be successful. In a few instances enough improvement has followed their use to warrant further trial.

## VAGINAL HYSTERECTOMY—WEIGHT OF NEWBORN

***To the Editor:***—**I would appreciate any information on the following: 1. Who performed the first vaginal hysterectomy in America, and when? 2. What is the greatest authentic recorded weight of any newborn infant successfully delivered vaginally in this country? I find that Dr. O. O. Burgess of California delivered an 18 pound (8.2 Kg.) child in 1875. He appears to have accurately weighed and measured the newborn infant (*Pacific M. & S. J.* 9: 179, 1875.) Has this feat been excelled?**

**T. Richard Hofmann, M.D., Berkeley, Calif.**

ANSWER.—1. The only vaginal hysterectomy recorded in the American literature as having been performed prior to 1850, and therefore presumably the first vaginal hysterectomy performed in this country, is credited to Dr. J. Collins Warren. The date given is 1829. This reference is given by Dr. A. F. Lash (*Am. J. Obst. & Gynec.* **42**:452 [Sept.] 1941).

2. The largest newborn child delivered vaginally in this country that is recorded in the literature (Belcher, D. P.: A Child Weighing Twenty-Five Pounds at Birth, THE JOURNAL, Sept. 23, 1916, p. 950) was delivered by Dr. D. P. Belcher of Sale City, Ga. This was a 25 pound (11.3 Kg.) stillbirth. The type of scale used was not described. Koff and Potter in a recent article (Koff, A. K., and Potter, E. L.: *Am. J. Obst. & Gynec.* **38**:412 [Sept.] 1939) state that they were unable to find any authenticated instance of a living baby with a birth weight of 15 pounds (6.8 Kg.). However, in a discussion of this paper before the Chicago Gynecological Society, Dr. John A. C. Busby reported (*ibid.*, p. 422) a delivery at West Suburban Hospital of a baby weighing 16 pounds 3 ounces (7.4 Kg.). The infant was weighed on a certified beam scale and was living and well.

## REFRACTORY URINARY TRACT INFECTION

***To the Editor:***—**Two months ago a man who had an infected bladder from a large prostate had a transurethral resection (by a competent specialist), which seems to have relieved the obstruction. His urine is loaded with pus, the bladder capacity is about 50 cc. and he voids every half hour. The nonprotein nitrogen is 37.4, the blood pressure 142 systolic and 88 diastolic. The trouble seems to be local. Will you outline a proper method of treatment, as what I have used has seemed so ineffective?**

**Mervin T. Sudler, M.D., Lawrence, Kan.**

ANSWER.—First, attempts should be made to eradicate the infection of the urinary tract. Toward this end a specimen of catheterized urine should be examined by means of Gram's stain and culture; several samples of urine should be examined for the tubercle bacillus. Suitable chemotherapy should then be instituted and the particular drug to be employed will depend on the type of bacteria found. A member of the sulfonamide group or mandelic acid will be most efficacious. Vesical lavage with potassium permanganate (1: 8,000) may also be carried out. The presence of residual urine should be determined, and, in order to exclude urinary calculi, a plain roentgenogram of the urinary tract should be made.

If the patient fails to improve under this regimen a short course of prostatic massage should be given. Then if improvement does not result it will be necessary to carry out further urologic investigation. If an excretory urogram fails to reveal any lesion of the upper part of the urinary tract, cystoscopy should be performed. Careful search for urethral stricture, vesical calculi, interstitial or tuberculous cystitis, persistent infected prostatic tissue and diverticula should be made and proper therapy instituted.

## DERMATITIS VENENATA CAUSED BY ROACH POWDER

***To the Editor:***—**A woman aged 65, while engaged in cleaning, came in contact four months ago with a green paste which had been spread on a potato for the purpose of killing roaches in an apartment house. The paste is known as "J. O. Roach Paste," is manufactured by John Opitz, Inc., 50-14 Thirty-Ninth Street, Long Island City, N. Y., and has as its content 1.375 per cent phosphorus plus inert material. Three weeks after contact there was an ulcer the size of a dime (18 mm.) situated below the inner malleolus of the left ankle. There was considerable erythema and vesiculation of the entire ankle. She complained of itching, especially on the flexor surfaces of arms and legs and on the neck. This resembled the milder form of dermatitis venenata. It disappeared with the use of 1 cc. of epinephrine hydrochloride subcutaneously. The blood count was normal. The blood Wassermann reaction was negative. The patient continued to have flare-ups of generalized pruritus and erythema, especially about the antecubital fossa, and a papulovesicular dermatitis on the left leg and foot. The blood sugar was negative. Repeated tests of urine for sugar were negative. The symptoms subsided in the following two months. At the insistence of an insurance company she was hospitalized for three days for diagnostic study. Patch tests and skin biopsies were done and were claimed to be negative. Hospital reports on the cutaneous tests stated that they were positive for nonhemolytic Staphylococcus aureus. Scrapings taken from between the toes showed the fungus Trichophyton gypseum gasper. Skin biopsy was negative for lichen planus. The patch test was done the day before her discharge with roach paste and also a powder believed to be sodium fluoride. This was read negative the next morning; the patient was discharged on the next day. Following her return home in the afternoon and during the next day the patient experienced a gradual recurrence of her former symptoms, much more aggravated than at any time during which I had seen her. She had an acute angioneurotic edema which required morphine sulfate and epinephrine for relief, repeated two or three times. In the next few weeks she had a series of furuncles about the face, neck, chest and arms which did not respond in the usual manner and left scars after the removal of a greenish gray fibropurulent core. The dermatitis about the elbows and shins of the left leg become more and more eczematous. It is now nine weeks since this flare-up, but the patient still has recurrent furunculosis, now very mild, and she is improving. I would appreciate any information you can give me as to the proper procedure to follow.**

**M.D., New York.**

ANSWER.—There is some evidence that this patient was suffering from something more than a dermatitis venenata. The eruption with itching on the flexor surfaces of the arms and legs and on the neck that disappeared with the injection of epinephrine may have been urticaria. The angioneurotic edema experienced later supports this thought.

The erythema and vesiculation on the ankle surrounding an ulcer may have been due to contact with some irritant. This is merely a possibility. The information given leaves in doubt whether the ulcer was present prior to exposure to the roach powder. It seems doubtful that such a severe dermatitis could be produced on one leg without affecting the other unless there was prolonged and accidental contact at the one site. Such contact may lead to painful burns that are slow to heal, because phosphorus pentoxide and phosphoric acid are formed in the tissues. Their action can be neutralized by warm wet dressings of 5 per cent aqueous solution of sodium bicarbonate. One per cent aqueous copper sulfate solution is useful in a similar way.

"Phossy jaw" is osteitis, periostitis and necrosis of osseous tissue of the mandible, less often of the maxillas resulting from phosphorus poisoning. There are toothache, loosening of the teeth and inflammation of the alveolar processes with suppuration. The breath is garlic scented, and there is salivation. Phosphorus poisoning of the jaw does not take place unless there are carious teeth.

The deeper tissue changes, such as of the jaw, require a protracted contact with phosphorus. As to whether ulceration and irritation such as occurred in this patient after three weeks' exposure is possible is not certain. It is presumed that the patch tests that gave negative results were properly made. It would have been better if the sites for these tests had been inspected longer than for twenty-four hours, since in some cases there may be delayed reactions. Patch tests, though exceedingly useful, have many limitations. Among these is the fact that the conditions of an exposure to a noxious agent are not all fulfilled. May this woman have had such a combination in her home with the roach power which was not duplicated in the patch test with the roach powder alone? She promptly developed a dermatitis on her return home, when it may be supposed that the roach powder was removed as thoroughly as possible. If this is a real dermatitis venenata, investigation should not stop with only one suspected agent but should be extended to numbers of others also. It would serve academic interest at least to sprinkle in a limited way some of the roach powder about the house and then observe its effects.

## RETURN OF MENSTRUAL PERIODS AFTER SEVENTEEN YEARS

*To the Editor:*—**A patient aged 67 has begun a menstrual flow after a cessation (total) for seventeen years. The flow is bright red with a number of clots at different times. She is free of any discharge or bleeding between the periods, which come every three to four weeks and last about five days. In addition she has become aware of some sexual desire. She is a large, obese woman, weighing close to 300 pounds (135 Kg.), and pelvic examination is difficult. The vagina is atrophic and small, the cervix is barely palpable and free of any tumors or ulcers, the adnexa seem free, and palpation of the uterus or extraneous tumors cannot be made. Otherwise physically she seems to be in good health. Her one complaint is associated with a frequency and dysuria. Repeated urine samples have shown small amounts of pus from time to time. Antispasmodics relieve the bladder symptoms but not entirely. Is it possible that an ovary could become revitalized at that advanced age or could the pituitary have some influence? What further procedures would you advise for diagnosis and therapy?**

**Herbert J. Schwartz, M.D., Challis, Idaho.**

ANSWER.—This history suggests that the patient may have been receiving estrogenic medication. If such is not the case, there is probably a pelvic newgrowth involving the ovary. Despite the patient's age, it is essential that the exact condition of the pelvic viscera be determined. If examination under anesthesia, including diagnostic curettage, does not yield dependable and sufficient information, surgical exposure of the ovaries by the vaginal route is warranted in such an unusual case; abdominal exploration would evidently present too serious a hazard.

## PRURITUS WITH DRY SKIN

*To the Editor:*—**Please send available information on the gland or glands of internal secretion concerned in clearing up a case of long-standing dry, itching skin. The condition did not trouble the patient while she was pregnant and she remained free from the dry, itching skin during that time. Since the termination of pregnancy she has had the same dry, itching skin again. Pregnancy and menstruation are all the result of a balance of several glands, but which one in particular has control or lack of control on the skin of the body? She is not elderly, and kraurosis is excluded.**

**Ralph J. Petrucci, M.D., Warren, R. I.**

ANSWER.—Hypothyroidism is frequently concerned with the genesis of pruritus with a dry skin, and it is advisable to ascertain the basal metabolic rate of the patient and in addition to local treatment treat any hypothyroidism if present. Sevringhaus investigated the clinical significance of the various glands of internal secretion in relation to diseases produced by the variation in function of any of these glands (Endocrine Glands and Their Relations to Dermatology, *Arch. Dermat. & Syph.* **43**:763 [May] 1941). The appearance of various toxic dermatoses, erythemas, purpuras, herpes gestationis and the appearance or aggravation of the neurodermatoses is often noted in pregnancy. The possibility of pruritus hiemalis or its variant bath pruritus must also be considered in this case. These conditions are more common during the winter months, and in pruritus hiemalis there is more or less generalized itching, which appears during the winter and clears up during the summer. Bath pruritus is also more common during the winter months, and the itching in these cases occurs frequently after taking a bath and is not persistent. A general discussion of the casual factors in pruritus and a classification of a number of the etiologic possibilities are given by Wien, M. S.: Pruritus in Medicine and in Dermatology (*Illinois M. J.* **81**:125 [Feb.] 1942).

## HYDROCHLORIC ACID ADMINISTRATION AND GASTRIC ACIDITY

*To the Editor:*—**Will diluted hydrochloric acid U. S. P. in the usual size doses of 1 to 4 cc. really change the $p_H$ of the gastric secretions?**

**N. M. DeVaughn, M.D., Augusta, Ga.**

ANSWER.—It is generally agreed that the ordinary doses of diluted hydrochloric acid U. S. P. are ineffective in producing material change in the $p_H$ of the gastric contents. Kern, Rose and Austin showed that the 1 cc. dose failed to produce any free acid to Töpfer's reagent or any change in the $p_H$. Shay and Gershon-Cohen found that 5 cc. of diluted hydrochloric acid, when administered with an Ewald meal to persons with anacidity, failed to show free acid at any time during the test or $p_H$ readings in the free acid range, i. e. 3.5 or lower. Even the slight changes produced by large doses are evanescent in effect, owing to the buffering capacity of gastric mucus, to dilution changes and to emptying of the stomach.

It is exceedingly difficult to ascribe any improvement following the administration of diluted hydrochloric acid U. S. P. to changes produced in the acidity of the gastric contents.

References:

Kern, R. A.; Rose, Edward, and Austin J. H.: The Effect of Orally Administered Hydrochloric Acid on Gastric Contents in Normal Individuals and in Patients with Achlorhydria, *J. Clin. Investigation* **2**:545 (Aug.) 1926.

Shay, Harry, and Gershon-Cohen, Jacob: A Comparison of the Effectiveness of Glutamic Acid Hydrochloride and Dilute Hydrochloric Acid as the Replacement Therapy in Anacidity Measured by Fractional Gastric Acid Titration and Hydrogen Ion Concentration Curves, *Ann. Int. Med.* **9**:1628 (June) 1936.

## PROBABLE DENTAL FLUOROSIS

*To the Editor:*—**A fourteen year old girl has dead-white, brittle or friable teeth with none of the usual glistening enamel. What should be done and what is the probable cause? Temporarily I have advised calcium gluconate (since she cannot drink milk), vitamin C and, to some extent, vitamin D. She may need riboflavin or vitamin A or both; I do not know. There is no evidence of endocrine disturbances.**

**Matthew Karasek, M.D., Shidler, Okla.**

ANSWER.—It would appear that the case described is one of a mild to moderate dental fluorosis caused by the use of a domestic water containing excessive amounts of fluorides during the period of tooth development (Dean, H. T.: Chronic Endemic Dental Fluorosis, THE JOURNAL, Oct. 17, 1936, p. 1269). As this hypocalification occurs during the time of amelification, the posteruptive therapy outlined would not be expected to improve the condition. Assuming that this is a case of dental fluorosis, the domestic water used by this person during the first eight years of life should be checked for its fluoride content in order to obviate the further development of similar conditions in other children.

## GLASSES FOR READING IN SUNLIGHT

*To the Editor:*—**Are there any glasses which are considered suitable for reading in the bright sunlight? Can corrections be incorporated in such glasses?**

**M.D., Illinois.**

ANSWER.—Any glass that reduces the total amount of light coming to the eye can be used for reading in bright sunlight. Most of the leading optical manufacturers have some patented dark glass in which suitable correction can be ground. Despite extensive claims, however, no one glass has been established as possessing qualities that mark it as definitely superior to others.

## VARYING RESPONSE OF GONORRHEA TO SULFATHIAZOLE

*To the Editor:*—**Is there any basis for the theory that the blood type has anything to do with the response of a patient to sulfonamide therapy or with the occurrence of undesirable reactions? Is there any explanation why some patients with gonorrhea for example, are cured promptly by sulfathiazole and others not at all?**

**M.D., M. C., U. S. Navy.**

ANSWER.—There is no evidence that blood type has anything to do with the response of a patient to sulfonamide therapy or to the occurrence of toxic reactions. The best explanation of the sulfathiazole treatment of gonorrhea is a difference in susceptibility of different strains of gonococci to the drug.

# JOURNALS ABSTRACTED IN THE CURRENT MEDICAL LITERATURE DEPARTMENT, MAY-AUGUST 1942

Titles have been listed or Abstracts made of important articles in the following journals in the Current Literature Department of THE JOURNAL during the past four months. Any of the journals, except those starred, will be lent by THE JOURNAL to subscribers in continental United States and Canada and to members of the American Medical Association for a period not exceeding three days. Three journals may be borrowed at a time. No journals are available prior to 1932. Requests for periodicals should be addressed to the Library of the American Medical Association and should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Thus most of these journals are accessible to the general practitioner.

Acta chirurgica Scandinavica. Stockholm.
Acta dermato-venereologica. Stockholm.
American Heart Journal. St. Louis.
American Journal of Clinical Pathology. Baltimore.
American Journal of Digestive Diseases. Fort Wayne, Ind.
*American Journal of Diseases of Children. A. M. A., Chicago.
American Journal of Hygiene. Baltimore.
American Journal of the Medical Sciences. Philadelphia.
American Journal of Obstetrics and Gynecology. St. Louis.
American Journal of Ophthalmology. Cincinnati.
American Journal of Orthodontics and Oral Surgery. St. Louis.
American Journal of Orthopsychiatry. Menasha, Wis.
American Journal of Pathology. Ann Arbor, Mich.
American Journal of Physiology. Baltimore.
American Journal of Psychiatry. New York.
American Journal of Public Health. New York.
American Journal of Roentgenol. and Radium Therapy. Springfield, Ill.
American Journal of Surgery. New York.
American Journal of Syphilis, Gonor. and Venereal Diseases. St. Louis.
American Journal of Tropical Medicine. Baltimore.
American Review of Tuberculosis. New York.
Anais brasileiros de ginecologia. Rio de Janeiro.
Anais paulistas de medicina e cirurgia. São Paulo.
Anales del Dispensario público nacional para enfermedades del aparato digestivo. Buenos Aires.
Anales del Instituto de investigaciones físicas aplicadas a la patología humana. Buenos Aires.
Anales del Instituto modelo de clínica médica. Buenos Aires.
Anesthesiology. New York.
Annals of Internal Medicine. Lancaster, Pa.
Annals of Otology, Rhinology and Laryngology. St. Louis.
Annals of Rheumatic Diseases. London.
Annals of Surgery. Philadelphia.
Archiv für Dermatologie und Syphilis. Berlin.
Archiv für die gesamte Physiologie. Berlin.
Archiv für klinische Chirurgie. Berlin.
Archiv für Psychiatrie und Nervenkrankheiten. Berlin.
*Archives of Dermatology and Syphilology. A. M. A., Chicago.
Archives of Disease in Childhood. London.
*Archives of Internal Medicine. A. M. A., Chicago.
*Archives of Neurology and Psychiatry. A. M. A., Chicago.
*Archives of Ophthalmology. A. M. A., Chicago.
*Archives of Otolaryngology. A. M. A., Chicago.
*Archives of Pathology. A. M A., Chicago.
Archives of Physical Therapy. Chicago.
*Archives of Surgery. A. M. A., Chicago.
Archivos argentinos de enfermedades del aparato digestivo y de la nutrición. Buenos Aires.
Archivos argentinos de pediatría. Buenos Aires.
Archivo del Hospital de niños Roberto del Río. Santiago.
Archivos de medicina infantil. Havana.
Archivos de medicina interna. Havana.
Archivos de pediatría del Uruguay. Montevideo.
Archivos uruguayos de medicina, cirugía y especialidades. Montevideo.
Arquivos de biologia. São Paulo.
Beiträge zur Klinik der Tuberkulose. Berlin.
Beiträge zur klinischen Chirurgie. Berlin.
Boletín de la Asociación médica de Puerto Rico. Santurce.
Boletín clínico. Medellín.
Boletín de la Sociedad chilena de obstetricia y ginecología. Santiago.
Boletín de la Sociedad cubana de pediatría. Havana.
Boletín de la Sociedad de obstetricia y ginecología de Buenos Aires.
Brain. London.
Brasil-medico. Rio de Janeiro.
British Heart Journal. London.
British Journal of Anæsthesia. Manchester.
British Journal of Children's Diseases. London.
British Journal of Dermatology and Syphilis. London.
British Journal of Experimental Pathology. London.
British Journal of Ophthalmology. London.
British Journal of Radiology. London.
British Journal of Surgery. Bristol.
British Journal of Tuberculosis. London.
British Journal of Urology. London.
British Medical Journal. London.

*Cannot be lent.

Bulletin of the Health Organization of the League of Nations. Geneva.
Bulletin of the Johns Hopkins Hospital. Baltimore.
Bulletin of the New York Academy of Medicine. New York.
California and Western Medicine. San Francisco.
Canadian Medical Association Journal. Montreal.
Canadian Public Health Journal. Toronto.
Cancer Research. Baltimore.
Cardiologia. Basel.
Chirurg. Berlin.
Connecticut State Medical Journal. Hartford.
Delaware State Medical Journal. Wilmington.
Der deutsche Militärarzt. Berlin.
Deutsche Zeitschrift für Nervenheilkunde. Berlin.
Dia médico. Buenos Aires.
Edinburgh Medical Journal.
Endocrinology. Springfield, Ill.
Geneeskundig tijdschrift voor Nederlandsch-Indië. Batavia.
Glasgow Medical Journal.
Guy's Hospital Reports. London.
Hawaii Medical Journal. Honolulu.
Helvetica medica acta. Basel.
Hospital. Rio de Janeiro.
Illinois Medical Journal. Chicago.
Indian Medical Gazette. Calcutta.
Irish Journal of Medical Science. Dublin.
Journal of Allergy. St. Louis.
Journal of the Arkansas Medical Society. Fort Smith.
Journal of Aviation Medicine. St. Paul.
Journal of Bone and Joint Surgery. Boston.
Journal of Clinical Endocrinology. Springfield, Ill.
Journal of Clinical Investigation. New York.
Journal of Endocrinology. London.
Journal of Experimental Medicine. New York.
Journal of the Florida Medical Association. Jacksonville.
Journal of Hygiene. London.
Journal of Immunology. Baltimore.
Journal of the Indiana State Medical Association. Indianapolis.
Journal of Industrial Hygiene and Toxicology. Baltimore.
Journal of Infectious Diseases. Chicago.
Journal of Investigative Dermatology. Baltimore.
Journal of the Iowa State Medical Society. Des Moines.
Journal of the Kansas Medical Society. Topeka.
Journal of Laboratory and Clinical Medicine. St. Louis.
Journal-Lancet. Minneapolis.
Journal of Laryngology and Otology. London.
Journal of the Maine Medical Association. Portland.
Journal of the Medical Association of the State of Alabama. Montgomery.
Journal of the Medical Association of Georgia. Atlanta.
Journal of the Medical Society of New Jersey. Trenton.
Journal of Mental Science. London.
Journal of the Michigan State Medical Society. Muskegon.
Journal of the Missouri State Medical Association. St. Louis.
Journal of the Mount Sinai Hospital. New York.
Journal of the National Cancer Institute. Washington, D. C.
Journal of Nervous and Mental Disease. New York.
Journal of Neurology and Psychiatry. London.
Journal of Neuropathology and Experimental Neurology. Baltimore.
Journal of Neurophysiology. Springfield, Ill.
Journal of Nutrition. Philadelphia.
Journal of Obstetrics and Gynaecology of British Empire. Manchester.
Journal of the Oklahoma State Medical Association. Oklahoma City.
Journal of Pathology and Bacteriology. Edinburgh.
Journal of Pediatrics. St. Louis.
Journal of Pharmacology and Experimental Therapeutics. Baltimore.
Journal of Physiology. Cambridge.
Journal of the Royal Naval Medical Service. London.
Journal of the South Carolina Medical Association. Florence.
Journal of the Tennessee State Medical Association. Nashville.
Journal of Thoracic Surgery. St. Louis.
Journal of Urology. Baltimore.
Kentucky Medical Journal. Bowling Green.
Klinische Wochenschrift. Berlin.
Lancet. London
Laryngoscope. St. Louis.
Lisboa médica. Lisbon.
Medical Annals of the District of Columbia. Washington.
Medical Journal of Australia. Sydney.

Medicina. Buenos Aires.
Medicina española. Valencia.
Medicine. Baltimore.
Memorias do Instituto Butantan. São Paulo.
Memorias do Instituto Oswaldo Cruz. Rio de Janeiro.
Military Surgeon. Washington, D. C.
Minnesota Medicine. St. Paul.
Monatsschrift für Geburtshilfe und Gynäkologie. Basel.
Monatsschrift für Kinderheilkunde. Berlin.
Monatsschrift für Unfallheilkunde. Berlin.
Münchener medizinische Wochenschrift. Munich.
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# SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "OS," Organization Section; "SS," Student Section; "ab," abstracts; the star (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." State board examinations are entered under the general heading State Board Reports, and not under the names of the individual states. Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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*Acad.*—*Academy*
*Am.*—*American*
*A.*—*Association*
*Coll.*—*College*
*Conf.*—*Conference*
*Cong.*—*Congress*
*Conv.*—*Convention*
*Dist.*—*District*
*Hosp.*—*Hospital*
*Internat.*—*International*
*M.*—*Medical*
*Med.*—*Medicine*
*Nat.*—*National*
*Pharm.*—*Pharmaceutical*
*Phys.*—*Physicians*
*Rev.*—*Revision*
*Ry.*—*Railway*
*Soc.*—*Society*
*Surg.*—*Surgery*
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